EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	89	514/2.ccls. and antitumor SAME peptide	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2007/09/04 15:43
S20	1	"200236145".did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 10:54
S21	4	"2003033012".did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 12:09
S22	2	"6274551".did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 11:59
S23	0	"6274551".did. and methylhexyl	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 11:59
S24	0	"6274551".did. and (analogue or analog)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 11:59
S25	0	"6274551".did. and (analogue or analog or derivative)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 11:59
S26	2	"20040067895".did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 12:09
S27	0	"20040067895".did. and methylhexyl	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 12:09

EAST Search History

S28	0	"20040067895".did. and hexyl	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 12:09
S29	0	"20040067895".did. and methyl	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 12:09
S30	1	"20040067895".did. and analog	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 12:10
S31	1	"20040067895".did. and derivative	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/09/29 13:37

REVIEW FURTHER

Subsequence search history

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=> d his L8

     (FILE 'HCAPLUS, USPATFULL' ENTERED AT 09:17:18 ON 04 SEP 2007)
L8            57 S L3 NOT L7

=> d que L8
L1            94 SEA FILE=REGISTRY ABB=ON  PLU=ON  VTVVP'ORN'ITIVFXV/SQSP
L2            81 SEA L1
L3            64 SEA L2 AND (PY<2004 OR AY<2004 OR PRY<2004 OR REVIEW/DT)
L5            64 SEA ("FAIRCLOTH GLYNN"/AU OR "FAIRCLOTH GLYNN T"/AU OR
                   "FAIRCLOTH GLYNN T JR"/AU OR "FAIRCLOTH GLYNN THOMAS"/AU)
L6             1 SEA "MARCHANTE MARIA DEL CARMEN CUEVAS"/AU
L7            64 SEA L5 OR L6
L8            57 SEA L3 NOT L7
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Subsequence search results

=> d ibib ed ab

L10 ANSWER 1 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:868555 HCAPLUS Full-text
DOCUMENT NUMBER: 146:219719
TITLE: Kahalalide F and ES285: potent anticancer agents from marine molluscs
AUTHOR(S): Faircloth, G.; Cuevas, C.
CORPORATE SOURCE: PharmaMar SA, Madrid, 28770, Spain
SOURCE: Progress in Molecular and Subcellular Biology (2006), 43(Molluscs), 363-379
CODEN: PMSBA4; ISSN: 0079-6484
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 28 Aug 2006
AB A review. The marine environment is proving to be a very rich source of unique compds. with significant activities against cancer of several types. Finding the sources of these new chemical entities has made it necessary for marine and medical scientists to find enterprising ways to collaborate in order to sample the great variety of intertidal, shallow and deep-water sea life. Recently these efforts resulted in a first generation of drugs from the sea undergoing clin. trials. These include PharmaMar compds.: Yondelis, Aplidin, kahalalide F, ES285 and Zalypsis. Two of these compds., kahalalide F and ES285, have been isolated from the Indopacific mollusc Elysia rufescens and the North Atlantic mollusc Spisula polynyma, resp.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d L10 2-56 ibib ed ab

L10 ANSWER 2 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:213791 HCAPLUS Full-text
DOCUMENT NUMBER: 145:179914
TITLE: Adding pharmacogenomics to the development of new marine-derived anticancer agents
AUTHOR(S): Jimeno, Jose; Aracil, Miguel; Tercero, Juan Carlos
CORPORATE SOURCE: PharmaMar R and D, Madrid, Spain
SOURCE: Journal of Translational Medicine (2006), 4, No pp. given
CODEN: JTMOBV; ISSN: 1479-5876
URL: http://www.translational-medicine.com/content/pdf/1479-5876-4-3.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; General Review; (online computer file)
LANGUAGE: English
ED Entered STN: 09 Mar 2006
AB A review. Nature has always been a highly productive tool in the development of anticancer therapies. Renewed interest in the potential of this tool has recently been sparked by the realization that the marine ecosystem can be used for the discovery and development of new compds. with clin. potential in advanced resistant tumors. These compds. can be incorporated into combination approaches in a chronic therapy scenario. Our marine anticancer program is using the sea to develop new agents with activity in resistant solid tumors and to identify new cellular targets for therapeutic intervention. This review describes the integration of different pharmacogenomic tools in the

development of Yondelis, Aplidin and Kahalalide F, three marine-derived compds. currently in Phase II or III development. Our results are reinforcing the targeted selectivity of these agents and opening the gates for customized therapies in cancer patients in the near future.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:100738 HCAPLUS Full-text
DOCUMENT NUMBER: 144:198849
TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients
INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar
PATENT ASSIGNEE(S): India
SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006024365	A1	20060202	US 2005-134633	20050519 <--
IN 2002MU00697	A	20040529	IN 2002-MU697	20020805 <--
IN 193042	A1	20040626		
IN 2002MU00699	A	20040529	IN 2002-MU699	20020805 <--
IN 2003MU00080	A	20050204	IN 2003-MU80	20030122 <--
IN 2003MU00082	A	20050204	IN 2003-MU82	20030122 <--
US 2004096499	A1	20040520	US 2003-630446	20030729 <--

PRIORITY APPLN. INFO.:

IN 2002-MU697	A	20020805 <--
IN 2002-MU699	A	20020805 <--
IN 2003-MU80	A	20030122 <--
IN 2003-MU82	A	20030122 <--
US 2003-630446	A2	20030729 <--

ED Entered STN: 03 Feb 2006
AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.

L10 ANSWER 4 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1321640 HCAPLUS Full-text
DOCUMENT NUMBER: 145:116379
TITLE: Ecteinascidin 743 (ET-743; Yondelis), aplidin, and kahalide F
AUTHOR(S): Henriquez, Ruben; Faircloth, Glynn; Cuevas, Carmen
CORPORATE SOURCE: PharmaMar, Madrid, 28770, Spain
SOURCE: Anticancer Agents from Natural Products (2005), 215-240, 2 plates. Editor(s): Cragg, Gordon M.; Kingston, David G. I.; Newman, David J. CRC Press LLC: Boca Raton, Fla.
CODEN: 69HQQY; ISBN: 0-8493-1863-7

DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
ED Entered STN: 20 Dec 2005
AB A review on the first generation of drugs isolated from marine organisms, i.e., Ecteinascidin 743, Aplidin, and Kahalide F. Topics discussed include their origin, mechanisms of action, chemical synthesis, drug development, and clin. studies.
REFERENCE COUNT: 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:540495 HCAPLUS Full-text
DOCUMENT NUMBER: 143:48021
TITLE: Solvent for biogenic active pharmaceutical ingredients derived from toxins
INVENTOR(S): Weickmann, Dirk
PATENT ASSIGNEE(S): Toximed G.m.b.H., Germany
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056027	A2	20050623	WO 2004-DE2713	20041210 <--
WO 2005056027	A3	20050721		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10357970	A1	20050707	DE 2003-10357970	20031211 <--
EP 1699473	A2	20060913	EP 2004-802918	20041210 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

PRIORITY APPLN. INFO.: DE 2003-10357970 A 20031211 <--
WO 2004-DE2713 W 20041210

ED Entered STN: 23 Jun 2005
AB The invention relates to a solvent for biogenic active pharmaceutical ingredients, which is basically comprised of the following components: (a) 7 mL of the homeopathic substance Tarantula D4 intermingled in 15 mL of a 0.9 % NaCl solution as basic component; (b) up to 0.5 of a saturated solution of the entire poisonous cocktail from spiders of the species Loxosceles laeta, or Loxosceles gaucho, or Loxosceles Mallorca, or Loxosceles Menorca is added to the basic component, (c) the entire poisonous cocktail is ground into an anhydrous formic acid depending on the required quant. proportions, 1 to 2 mL of the entire exts. of poisons of bulldog ants being in turn added thereto, wherein said amount relates to a total amount of 10 mL of the entire poisonous cocktail.

L10 ANSWER 6 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:409543 HCAPLUS Full-text
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2005042558	A1	20050512	WO 2004-CA1902		20041029	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW						
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
US 2005148535	A1	20050707	US 2004-975974		20041028	<--
CA 2542904	A1	20050512	CA 2004-2542904		20041029	<--
EP 1682565	A1	20060726	EP 2004-789809		20041029	<--
R: DE, FR, GB						
JP 2007510408	T	20070426	JP 2006-537024		20041029	<--
PRIORITY APPLN. INFO.:			US 2003-516192P	P	20031030	<--
			WO 2004-CA1902	W	20041029	

ED Entered STN: 13 May 2005
AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).

L10 ANSWER 7 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:409357 HCAPLUS Full-text
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of

proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119217	A1	20050602	US 2004-975790	20041028 <--
AU 2004284855	A1	20050512	AU 2004-284855	20041029 <--
CA 2542884	A1	20050512	CA 2004-2542884	20041029 <--
EP 1691842	A1	20060823	EP 2004-789807	20041029 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004015779	A	20061226	BR 2004-15779	20041029 <--
CN 1901939	A	20070124	CN 2004-80039601	20041029 <--
JP 2007509861	T	20070419	JP 2006-537023	20041029 <--
IN 2006MN00614	A	20070420	IN 2006-MN614	20060526 <--
NO 2006002420	A	20060731	NO 2006-2420	20060529 <--
PRIORITY APPLN. INFO.:			US 2003-516263P P	20031030 <--
			WO 2004-CA1900 W	20041029

ED Entered STN: 13 May 2005

AB The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:283298 HCAPLUS Full-text

DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005027842	A2	20050331	WO 2004-US30368		20040916 <--
WO 2005027842	A3	20051222			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
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US 2004154316	A1	20040812	US 2003-359834		20030207 <--
CA 2515188	A1	20040826	CA 2004-2515188		20040203 <--
WO 2004072913	A2	20040826	WO 2004-US3021		20040203 <--
WO 2004072913	A3	20041111			
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EP 1590776	A2	20051102	EP 2004-707767		20040203 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2004007281	A	20060131	BR 2004-7281		20040203 <--
CN 1754192	A	20060329	CN 2004-80005053		20040203 <--
AU 2004273910	A1	20050331	AU 2004-273910		20040916 <--
CA 2538570	A1	20050331	CA 2004-2538570		20040916 <--
EP 1670477	A2	20060621	EP 2004-788798		20040916 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004014568	A	20061107	BR 2004-14568		20040916 <--
CN 1878556	A	20061213	CN 2004-80033294		20040916 <--
JP 2007505914	T	20070315	JP 2006-527024		20040916 <--
MX 2005PA08325	A	20060228	MX 2005-PA8325		20050805 <--
MX 2006PA03066	A	20060620	MX 2006-PA3066		20060317 <--
NO 2006001325	A	20060606	NO 2006-1325		20060323 <--
PRIORITY APPLN. INFO.:			US 2003-504310P	P	20030918 <--
			US 2003-359834	A	20030207 <--
			WO 2004-US3021	W	20040203

WO 2004-US30368 W 20040916

OTHER SOURCE(S): MARPAT 142:349042
ED Entered STN: 01 Apr 2005
AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

L10 ANSWER 9 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:239012 HCAPLUS Full-text
DOCUMENT NUMBER: 142:298335
TITLE: Preparation of kahalalide F analogs as antitumor agents
INVENTOR(S): Albericio Palomera, Fernando; Fernandez Donis, Ariadna; Giralt Lledo, Ernest; Gracia Cantador, Carolina; Lopez Rodriguez, Pilar; Varon Colomer, Sonia; Cuevas Marchante, Carmen; Lopez Macia, Angel; Francesch Solloso, Andres; Jiminez Garcia, Jose-Carlos; Royo Exposito, Miriam
PATENT ASSIGNEE(S): Pharma Mar, S.A.U., Spain; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023846	A1	20050317	WO 2004-GB3847	20040909 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004270471	A1	20050317	AU 2004-270471	20040909 <--
CA 2537128	A1	20050317	CA 2004-2537128	20040909 <--
EP 1664093	A1	20060607	EP 2004-768394	20040909 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1849333	A	20061018	CN 2004-80025890	20040909 <--
IN 2006DN01258	A	20070803	IN 2006-DN1258	20060308 <--
MX 2006PA02741	A	20060605	MX 2006-PA2741	20060309 <--
US 2007117743	A1	20070524	US 2006-570734	20061018 <--
PRIORITY APPLN. INFO.:			GB 2003-21066 A	20030909 <--
			WO 2004-GB3847 W	20040909

OTHER SOURCE(S): MARPAT 142:298335
ED Entered STN: 18 Mar 2005
AB The invention relates to new analogs of kahalalide F in which one or more exocyclic or cyclic amino acids has been substituted by other natural or nonnatural amino acids, masked with organic groups, or been removed or in which the terminal 5-methylhexanoyl (5-MeHex) group has by substituted by other acyl groups or been removed. Thus, [(4S)-MeHex14]-kahalalide F was

prepared by the solid-phase method and assayed for cytotoxic activity against various cell lines.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:95095 HCAPLUS Full-text
DOCUMENT NUMBER: 143:52574
TITLE: Technology evaluation: Kahalalide F, PharmaMar
AUTHOR(S): Hamann, Mark T.
CORPORATE SOURCE: The School of Pharmacy and Department of Chemistry and Biochemistry, University of Mississippi, MS, 38677, USA
SOURCE: Current Opinion in Molecular Therapeutics (2004), 6(6), 657-665
CODEN: CUOTFO; ISSN: 1464-8431
PUBLISHER: Thomson Scientific
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 03 Feb 2005
AB A review. Kahalalide F is a depsipeptide under development by PharmaMar as a potential treatment for solid tumors. It is currently undergoing phase II clin. trials.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:34709 HCAPLUS Full-text
DOCUMENT NUMBER: 142:100283
TITLE: Combination of hemocyanin from spiders with dolastatine form Dolabella for the treatment of prostate cancer
INVENTOR(S): Weickmann, Dirk
PATENT ASSIGNEE(S): Toximed G.m.b.H., Germany
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005002494	A2	20050113	WO 2004-DE1386	20040701 <--
WO 2005002494	A3	20050224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10329847	A1	20050120	DE 2003-10329847	20030702 <--

PRIORITY APPLN. INFO.: DE 2003-10329847 A 20030702 <--
ED Entered STN: 14 Jan 2005

AB The invention concerns a combination of (a) hemocyanin from the hemolymphs of certain bird-eating spiders; (b) substances that are antagonists, synergists, and penetration enhancers to hemocyanin and that are obtained from the fractionation of spider venoms; (c) dolastatine form Dolabella auricularia or a preparation named Kahalalide F from Elysia rufescens. Hemocyanine, antagonists, synergists, and penetration enhancers are isolated by various chromatog. methods; the fractions or their mixts. are lyophilized for storage. For formulation, isotonic solution, buffer, albumin, glutamine, antimicrobial agent, etc. are added.

L10 ANSWER 12 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:354967 HCAPLUS Full-text
DOCUMENT NUMBER: 140:357671
TITLE: Preparation of kahalalide antitumoral compounds
INVENTOR(S): Faircloth, Glynn Thomas; Elices, Mariano; Sasak, Halina; Aviles Marin, Pablo Manuel; Cuevas Marchante, Maria Del Carmen
PATENT ASSIGNEE(S): Pharma Mar, S.A.U., Spain
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035613	A2	20040429	WO 2003-US33207	20031020 <--
WO 2004035613	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003033012	A1	20030424	WO 2002-GB4735	20021018 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501089	A1	20040429	CA 2003-2501089	20031020 <--
AU 2003285911	A1	20040504	AU 2003-285911	20031020 <--
BR 2003015489	A	20050823	BR 2003-15489	20031020 <--
EP 1572726	A2	20050914	EP 2003-779140	20031020 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006517195	T	20060720	JP 2005-501483	20031020 <--
MX 2005PA04133	A	20051005	MX 2005-PA4133	20050418 <--
NO 2005002379	A	20050715	NO 2005-2379	20050513 <--

US 2006234920	A1	20061019	US 2006-531533		20060425 <--
PRIORITY APPLN. INFO.:			WO 2002-GB4735	A	20021018 <--
			GB 2003-4367	A	20030226 <--
			GB 2003-14725	A	20030624 <--
			US 2001-348449P	P	20011019 <--
			WO 2001-GB4821	A	20011031 <--
			GB 2002-22409	A	20020926 <--
			WO 2003-US33207	W	20031020 <--

ED Entered STN: 30 Apr 2004

AB The invention is directed to new kahalalide antitumoral compds., in particular to analogs of kahalalide F, which are useful as antitumoral, antiviral and antifungal agents and in the treatment of psoriasis. Thus, kahalalide F analogs in which the 5-methylhexanoc acid residue has been replaced by (S)- and (R)-4-methylhexanoic acid were prepared and assayed for cytotoxic activity against various cell lines.

L10 ANSWER 13 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:28665 HCAPLUS Full-text

DOCUMENT NUMBER: 141:140738

TITLE: Conformational analysis of natural marine cyclopeptides with anti-tumor properties

AUTHOR(S): Giralt, Ernest; Gairi, Margarida; Salvatella, Xavier; Rodriguez-Mias, Ricard Aleix; Jimenez, Jose Carlos; Lopez-Macia, Angel; Caba, Josep Maria; Cardenas, Francisco; Feliz, Miguel; Lloyd-Williams, Paul; Albericio, Fernando

CORPORATE SOURCE: Institut de Recerca Biomedica de Barcelona (IRBB-PCB), Universitat de Barcelona, Barcelona, 08028, Spain

SOURCE: Peptides 2002, Proceedings of the European Peptide Symposium, 27th, Sorrento, Italy, Aug. 31-Sept. 6, 2002 (2002), 758-759. Editor(s): Benedetti, Ettore; Pedone, Carlo. Edizioni Ziino: Castellammare di Stabia, Italy.
CODEN: 69EYXG; ISBN: 88-900948-1-8

DOCUMENT TYPE: Conference

LANGUAGE: English

ED Entered STN: 14 Jan 2004

AB A symposium report. Conformations of three natural marine cyclopeptides (aplidine, kahalalide F and trunkamide A) with antitumor properties are studied using NMR and mol. dynamics calcns. Aplidine exists in CHCl3 as an approx. 1:1 mixture of two slowly interconverting conformations. These conformational changes have no implications in the conformation of the ring that is a very well-defined eight-shaped macrocycle stabilized by a transannular hydrogen bond. Kahalalide F, a depsipeptide, has a flexible tail and a quite rigid macrocycle. Conformation of trunkamide A is observed to be very rigid, dominated by the volume of the dimethylallyl side chains, includes two trans-annular hydrogen bonds, and has two conformationally-restricted residues in the primary structure.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:861296 HCAPLUS Full-text

DOCUMENT NUMBER: 140:77392

TITLE: Stereochemistry of Kahalalide F

AUTHOR(S): Bonnard, Isabelle; Manzanares, Ignacio; Rinehart, Kenneth L.

CORPORATE SOURCE: Roger Adams Laboratory, Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana,

IL, 61801, USA
SOURCE: Journal of Natural Products (2003), 66(11), 1466-1470
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:77392
ED Entered STN: 04 Nov 2003
AB The stereochem. of the amino acids in the marine-derived cyclic depsipeptide kahalalide F has been defined by a series of degradation reactions (hydrolysis, ozonolysis, Edman degradation, and Marfey derivatization), yielding smaller fragments of the marine natural product. The results from these reactions agree with the structure originally proposed by Hamann and Scheuer and with the same stereochem. of most of the component amino acids more recently proposed by Goetz, Yoshida, and Scheuer. However, our assignments of D-Val3 and L-Val4 are the reverse of previous assignments made as L-Val3 and D-Val4. The present (reversed) stereochem. is crucial for the antitumor activity of kahalalide F.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:848751 HCAPLUS Full-text
DOCUMENT NUMBER: 140:385585
TITLE: In vitro toxicity of three new antitumoral drugs (trabectedin, aplidin, and kahalalide F) on hematopoietic progenitors and stem cells
AUTHOR(S): Gomez, Susana G.; Bueren, Juan A.; Faircloth, Glynn T.; Jimeno, Jose; Albella, Beatriz
CORPORATE SOURCE: PharmaMar, Madrid, Spain
SOURCE: Experimental Hematology (New York, NY, United States) (2003), 31(11), 1104-1111
CODEN: EXHMA6; ISSN: 0301-472X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Oct 2003
AB Objective: In addition to neutropenias and/or thrombocytopenias as a short-term effect, antineoplastics also can produce long-term effects as a consequence of damage to the hematopoietic stem cells. The aim of the present study was to evaluate the toxicity of three marine-derived antineoplastics on murine hematopoietic stem cells. These antitumoral compds. currently are being evaluated in patients in phase II (aplidin and kahalalide F) and phase II/III (trabectedin) clin. trials. Materials and methods: Long-term competitive repopulating assays were performed in mice to analyze toxic effects on the hematopoietic stem cells responsible for the multipotential long-term repopulation of hematopoiesis. Furthermore, granulocytic and T- and B-lymphoid lineages were studied, as well as myeloid (CFU-GM) and megakaryocytic (CFU-Meg) progenitors. Results: When cells were treated in vitro for 24 h with CFU-GM IC50 dose of trabectedin (9.59 ± 4.96 nM), no significant effects were observed in the stem cells. The dose of trabectedin that produced 90% of inhibition in CFU-GM (IC90: 23.71 ± 1.27 nM) only inhibited 45% survival of stem cells. Doses of aplidin that produced redns. of 50% (56.9 ± 13.32 nM) or 90% (195.88 ± 21.39 nM) in myeloid progenitors did not show any effect on hematopoietic stem cells. Kahalalide F did not show any toxic effect in either short-term or long-term repopulating cells up to 10 μM. Conclusions. Our data show that the hematopoietic stem cells effects of antitumoral drugs can be properly characterized by the murine competitive repopulating assays. Our results suggest that long-term myelosuppression as a

consequence of trabectedin, aplidin, or kahalalide F treatment would not be expected.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:800266 HCAPLUS Full-text
DOCUMENT NUMBER: 140:156903
TITLE: Kahalalide F, a new marine-derived compound, induces oncosis in human prostate and breast cancer cells
AUTHOR(S): Suarez, Yajaira; Gonzalez, Laura; Cuadrado, Ana; Berciano, Maite; Lafarga, Miguel; Munoz, Alberto
CORPORATE SOURCE: Pharma Mar S.A., Instituto de Investigaciones Biomedicas "Alberto Sols", Consejo Superior de Investigaciones Cientificas-Universidad Autonoma de Madrid, Madrid, Spain
SOURCE: Molecular Cancer Therapeutics (2003), 2(9), 863-872
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Oct 2003
AB Kahalalide F (KF) is a novel antitumor drug of marine origin under clin. investigation. KF showed a potent cytotoxic activity against a panel of human prostate and breast cancer cell lines, with IC50 ranging from 0.07 μM (PC3) to 0.28 μM (DU145, LNCaP, SKBR-3, BT474, MCF7). Importantly, nontumor human cells (MCF10A, HUVEC, HMEC-1, IMR90) were 5-40 times less sensitive to the drug (IC50 = 1.6-3.1 μM). KF cytotoxicity did not correlate with the expression level of the multidrug resistance MDR1 and of the Tyr kinase HER2/NEU, and only slightly by the anti-apoptotic BCL-2 protein. KF action was triggered rapidly by short pulse treatments (15 min caused 50% maximum cytotoxicity). Neither a general caspase inhibitor (Z-VAD-fmk) nor transcription or translation inhibitors (actinomycin D, cycloheximide) blocked KF action. Flow cytometry anal. revealed that KF induced neither cell-cycle arrest nor apoptotic hypodiploid peak. Using mitochondrial (JC-1)- and lysosomal (LysoTracker Green, Acridine Orange)-specific fluorophores, the authors detected loss of mitochondrial membrane potential and of lysosomal integrity following KF treatment. Confocal laser and electron microscopy revealed that KF-treated cells underwent a series of profound alterations including severe cytoplasmic swelling and vacuolization, dilation and vesiculation of the endoplasmic reticulum, mitochondrial damage, and plasma membrane rupture. In contrast, the cell nucleus showed irregular clumping of chromatin into small, condensed masses, while chromatin disappeared from other nuclear domains, but the nuclear envelope was preserved and no DNA degradation was detected. Together, these data indicate that KF induces cell death via oncosis preferentially in tumor cells.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:509479 HCAPLUS Full-text
DOCUMENT NUMBER: 140:146458
TITLE: Kahalalide F: synthesis and structural determination
AUTHOR(S): Lopez-Macia, Angel; Jimenez, Jose Carlos; Royo, Miriam; Giralt, Ernest; Albericio, Fernando
CORPORATE SOURCE: Department of Organic Chemistry, University of Barcelona, Barcelona, E-08028, Spain

SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 245-246. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr. CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 04 Jul 2003
AB A symposium report. Kahalalide F is a cyclic depsipeptide isolated from the Sacoglossan mollusc Elysia rufescens and the green alga Bryopsis sp. Kahalalide F and a diastereomer were prepared by the solid-phase method and their structures determined by 1H NMR.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:456011 HCAPLUS Full-text
DOCUMENT NUMBER: 139:390403
TITLE: Development of marine-derived anti-cancer compounds
AUTHOR(S): Taguchi, Tetsuo
CORPORATE SOURCE: Osaka University, Japan
SOURCE: Gan to Kagaku Ryoho (2003), 30(5), 579-588 CODEN: GTKRDX; ISSN: 0385-0684
PUBLISHER: Gan to Kagaku Ryohosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
ED Entered STN: 15 Jun 2003
AB A review. The marine environment offers a rich source of natural products with potential therapeutic application. Marine organisms have evolved the enzymic capability to produce potent chemical entitles that make them promising sources of innovative cytotoxic compds. Prominent in the identification and development of novel anti-cancer agents from marine sources is the Spanish biotechnol. company, Pharma Mar, which currently has a large number of oncol. products in late preclin. and clin. development. These include: Ecteinascidin-743 (ET-743), Aplidin, Kahalalide F and ES-285. Many of these innovative compds. have novel mechanisms of antitumor action that have yet to be fully elucidated.

L10 ANSWER 19 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:425678 HCAPLUS Full-text
DOCUMENT NUMBER: 140:111653
TITLE: Solid-phase synthesis of marine cyclic peptides with antitumoral activity
AUTHOR(S): Lopez-Macia, Angel; Caba, Josep M.; Jimenez, Jose C.; Salvatella, Xavier; Varon, Sonia; Royo, Miriam; Rodriguez, Ignacio; Manzanares, Ignacio; Giralt, Ernest; Albericio, Fernando
CORPORATE SOURCE: Department of Organic Chemistry, University of Barcelona, Barcelona, 08028, Spain
SOURCE: Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 7th, Southampton, United Kingdom, Sept. 18-22, 2001 (2002), Meeting Date 2001, 13-16. Editor(s): Epton, Roger. Mayflower Worldwide Ltd.: Kingswinford, UK.

CODEN: 69DYT7; ISBN: 0-9515735-4-3
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 04 Jun 2003
AB A symposium report. Two cyclic peptides, kahalalide F and trunkamide A, were prepared by the solid phase method and are currently in clin. phase I and preclin. trials for treatment of cancer, resp. Kahalalide F is a cyclic tridecapeptide containing an ester bond between two β-branched and sterically hindered amino acids, didehydroamino butyric acid, and a hydrophobic sequence with two fragments containing several β-branched amino acids in a row. Trunkamide A is a cyclic heptapeptide which contains hydroxy side-chain amino acids with the hydroxy function modified as dimethylallyl ethers and a thiazoline ring.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:319736 HCAPLUS Full-text
DOCUMENT NUMBER: 138:331673
TITLE: Kahalalide compounds for use in cancer therapy
INVENTOR(S): Jimeno, Jose; Lopez, Lazaro Luis; Ruiz Casado, Ana; Izquierdo, Miguel Angel; Paz-Ares, Luis; Trigo, Jose Manuel; Schellens, Jan
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033012	A1	20030424	WO 2002-GB4735	20021018 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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WO 2002036145	A2	20020510	WO 2001-GB4821	20011031 <--
WO 2002036145	A3	20021017		
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CA 2462639	A1	20030424	CA 2002-2462639	20021018 <--
AU 2002334203	A1	20030428	AU 2002-334203	20021018 <--
EP 1435990	A1	20040714	EP 2002-801430	20021018 <--

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        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
    CA 2501089          A1    20040429    CA 2003-2501089        20031020 <--
    WO 2004035613       A2    20040429    WO 2003-US33207        20031020 <--
    WO 2004035613       A3    20040729
        W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
            GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
            LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
            OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
            TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2003285911       A1    20040504    AU 2003-285911         20031020 <--
    BR 2003015489       A     20050823    BR 2003-15489          20031020 <--
    EP 1572726          A2    20050914    EP 2003-779140         20031020 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
    CN 1705677          A     20051207    CN 2003-80101647       20031020 <--
    JP 2006517195       T     20060720    JP 2005-501483         20031020 <--
    MX 2004PA03672      A     20050620    MX 2004-PA3672         20040419 <--
    US 2005054555       A1    20050310    US 2004-492670         20041103 <--
    ZA 2005002926       A     20060222    ZA 2005-2926           20050411 <--
    MX 2005PA04133      A     20051005    MX 2005-PA4133         20050418 <--
    NO 2005002379       A     20050715    NO 2005-2379           20050513 <--
PRIORITY APPLN. INFO.:                      US 2001-348449P    P  20011019 <--
                                            WO 2001-GB4821     A  20011031 <--
                                            GB 2002-22409      A  20020926 <--
                                            US 2000-244471P    P  20001031 <--
                                            US 2000-246229P    P  20001106 <--
                                            WO 2002-GB4735     W  20021018 <--
                                            GB 2003-4367       A  20030226 <--
                                            GB 2003-14725      A  20030624 <--
                                            WO 2003-US33207    W  20031020 <--
OTHER SOURCE(S):        MARPAT 138:331673
ED   Entered STN:  25 Apr 2003
AB   Procedures for clin. trials of kahalalide compds. are provided, leading to new
     formulations of kahalalide compds.
REFERENCE COUNT:        5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10  ANSWER 21 OF 56  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:       2002:779665  HCAPLUS  Full-text
DOCUMENT NUMBER:        138:313796
TITLE:                  Quantitative analysis of the novel depsipeptide
                        anticancer drug Kahalalide F in human plasma by
                        high-performance liquid chromatography under basic
                        conditions coupled to electrospray ionization tandem
                        mass spectrometry
AUTHOR(S):              Stokvis, E.; Rosing, H.; Lopez-Lazaro, L.; Rodriguez,
                        I.; Jimeno, J. M.; Supko, J. G.; Schellens, J. H. M.;
                        Beijnen, J. H.
CORPORATE SOURCE:       Department of Pharmacy and Pharmacology, Slotervaart
                        Hospital/The Netherlands Cancer Institute, Amsterdam,
                        1066 EC, Neth.
SOURCE:                 Journal of Mass Spectrometry (2002), 37(9),
                        992-1000
                        CODEN: JMSPFJ; ISSN: 1076-5174
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PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Oct 2002
AB Kahalalide F (KF) is a novel cyclic depsipeptide anticancer drug which has shown anticancer activity both in vitro and in vivo, especially against human prostate cancer cell lines. To characterize the pharmacokinetics of KF during a phase I clin. trial in patients with androgen-refractory prostate cancer, a method was developed and validated for the quant. anal. of KF in human plasma by HPLC coupled to pos. electrospray ionization tandem mass spectrometry (ESI-MS/MS). Microbore reversed-phase liquid chromatog. (LC) performed with mobile phases containing trifluoroacetic acid, an additive commonly used for separating peptides, resulted in substantial suppression of the signal for KF in ESI-MS/MS. An alternative approach employing a basic mobile phase provided an excellent response to KF when used in the pos. ion mode. Plasma samples were prepared for LC MS/MS by solid-phase extraction on C18 cartridges. The LC separation was performed on a Zorbax Extend C18 column (150 + 2.1 mm., particle size 5 μm) with MeCN-10 mM aqueous NH3 (85:15) as the mobile phase, at a flow-rate of 0.20 mL/min. A butyric acid analog of KF was used as the internal standard The lower limit of quantitation when using a 500-μL sample volume was 1 ng/mL and the linear dynamic range extended to 1000 ng/mL. The interassay accuracy of the assay was -15.1% at the lower limit of quantitation and between -2.68 and -9.05% for quality control solns. ranging in concentration from 2.24 to 715 ng/mL. The interassay precision was 9.91% or better at these concns. The analyte was stable in plasma under all conditions evaluated and for a period of 16 h after reconstituting plasma exts. for LC anal. at ambient temperature
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:742571 HCAPLUS Full-text
DOCUMENT NUMBER: 139:62716
TITLE: Preclinical toxicity studies of kahalalide F, a new anticancer agent: single and multiple dosing regimens in the rat
AUTHOR(S): Brown, Alan P.; Morrissey, Robert L.; Faircloth, Glynn T.; Levine, Barry S.
CORPORATE SOURCE: Toxicology Research Laboratory, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2002), 50(4), 333-340
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 01 Oct 2002
AB Kahalalide F (KF) is a new anticancer agent currently in clin. trials for solid tumors, including prostate cancer. During the preclin. development of this drug, the studies reported here were conducted to determine the acute and multiple dose toxicities of KF when administered i.v. to rats. This dosing route is the intended route of clin. administration. KF was administered i.v. to male and female CD rats using single- and multiple-dose (daily for 5 days) schedules. Animals were observed for clin. signs, and body weight, hematol., and clin. chemical parameters determined Animals were necropsied, gross observations and organ wts. recorded, and numerous tissues were collected and examined microscopically. KF produced lethality at 375 and 450 μg/kg in males and females, resp., and the maximum tolerated dose (MTD) was estimated to be 300 μg/kg (1800 μg/m2). The nervous system appeared to be a potential site of

action for the production of lethality. Single-dose administration of KF at 150 and 300 μg/kg produced organ toxicity in which the kidney was the primary target. Injury to distal convoluted tubules was the most toxicol. significant lesion, and was observed on day 4. However, by day 29, resolution of renal toxicity had occurred in the 150-μg/kg group, but only partial resolution was seen at 300 μg/kg. Renal injury correlated with increased serum creatinine, BUN, and kidney wts. at 300 μg/kg, indicating impairment of renal function. Subacute, necrotizing inflammation of bone marrow and peritrabecular osteocyte hyperplasia of bone were seen at 300 μg/kg on day 4, with recovery thereafter. Injury to blood vessels and surrounding tissue at the injection site were produced by KF, likely due to local cytotoxicity. In general, reversibility of toxicity was seen at 150 μg/kg but not at 300 μg/kg. When KF was administered once daily for five consecutive days at a dose of 80 μg/kg per day (400 μg/kg total dose), slightly decreased body weight gain was the primary drug-related effect. Therefore, the no-adverse-effect dose was at or near 80 μg/kg per day (480 μg/m2 per day). These findings demonstrate that fractionation of a lethal or MTD dose of KF by daily administration for 5 days reduces drug-induced toxicity, and appears to be a viable option for the clin. evaluation of KF for the treatment of cancer.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 23 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:692319 HCAPLUS Full-text
DOCUMENT NUMBER: 138:271948
TITLE: Solid-phase total syntheses of trunkamide A and kahalalide F, cyclic peptides of marine origin
AUTHOR(S): Albericio, Fernando; Caba, Josep M.; Lopez-Macia, Angel; Jimenez, Jose C.; Carrascal, Marta; Sole, Laia; Rodriguez, Ignacio; Manzanares, Ignacio; Royo, Miriam; Giralt, Ernest
CORPORATE SOURCE: Department of Organic Chemistry, University of Barcelona, Barcelona, E-08028, Spain
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 217-219. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL; ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 13 Sep 2002
AB A symposium report. Two cyclic peptides of marine origin, Trunkamide A and Kahalalide F, were synthesized. Common features of both syntheses include solid-phase peptide chain elongation using a quasi orthogonal protecting scheme with allyl, t-Bu, and fluorenyl based groups on a chlorotrityl resin.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:521462 HCAPLUS Full-text
DOCUMENT NUMBER: 137:88442
TITLE: Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
INVENTOR(S): Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S): Ire.

SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053138	A2	20020711	WO 2002-IE1	20020102 <--
WO 2002053138	A3	20020919		
W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG				
AU 2002219472	A1	20020716	AU 2002-219472	20020102 <--
EP 1351678	A2	20031015	EP 2002-727007	20020102 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004092583	A1	20040513	US 2004-250535	20040102 <--
PRIORITY APPLN. INFO.:			IE 2001-2 A	20010102 <--
			WO 2002-IE1 W	20020102 <--

OTHER SOURCE(S): MARPAT 137:88442
ED Entered STN: 12 Jul 2002
AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

L10 ANSWER 25 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:353299 HCAPLUS Full-text
DOCUMENT NUMBER: 136:359641
TITLE: Kahalalide F formulations for antitumor use
INVENTOR(S): Ruffles, Graham Keith; Faircloth, Glynn Thomas; Nuyen, Bastian; Weitman, Steve
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036145	A2	20020510	WO 2001-GB4821	20011031 <--
WO 2002036145	A3	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,				

IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2425627	A1	20020510	CA 2001-2425627		20011031 <--
AU 200210749	A	20020515	AU 2002-10749		20011031 <--
EP 1330258	A2	20030730	EP 2001-978654		20011031 <--
EP 1330258	B1	20051228			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001014912	A	20031014	BR 2001-14912		20011031 <--
JP 2004512370	T	20040422	JP 2002-538956		20011031 <--
CN 1568192	A	20050119	CN 2001-818271		20011031 <--
NZ 525243	A	20050128	NZ 2001-525243		20011031 <--
AT 314084	T	20060115	AT 2001-978654		20011031 <--
HU 200600031	A2	20060529	HU 2006-31		20011031 <--
ES 2256305	T3	20060716	ES 2001-1978654		20011031 <--
RU 2292216	C2	20070127	RU 2003-116124		20011031 <--
CA 2462639	A1	20030424	CA 2002-2462639		20021018 <--
WO 2003033012	A1	20030424	WO 2002-GB4735		20021018 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002334203	A1	20030428	AU 2002-334203		20021018 <--
EP 1435990	A1	20040714	EP 2002-801430		20021018 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
ZA 2003003136	A	20040723	ZA 2003-3136		20030423 <--
NO 2003001860	A	20030630	NO 2003-1860		20030425 <--
MX 2003PA03704	A	20040504	MX 2003-PA3704		20030425 <--
HK 1054192	A1	20060908	HK 2003-106441		20030910 <--
US 2004067895	A1	20040408	US 2003-399571		20031114 <--
PRIORITY APPLN. INFO.:			US 2000-244471P	P	20001031 <--
			US 2000-246229P	P	20001106 <--
			US 2001-348449P	P	20011019 <--
			WO 2001-GB4821	W	20011031 <--
			GB 2002-22409	A	20020926 <--
			WO 2002-GB4735	W	20021018 <--

ED Entered STN: 12 May 2002

AB New formulations and new uses of kahalalide F are provided for antitumor application against neuroblastomas or dedifferentiated or mesenchymal chondrosarcomas or osteosarcomas.

L10 ANSWER 26 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:924856 HCAPLUS Full-text

DOCUMENT NUMBER: 136:315111

TITLE: Development of an HPLC method with UV detection for the pharmaceutical quality control of the novel marine anticancer agent kahalalide F

AUTHOR(S): Nuijen, B.; Bouma, M.; Floriano, P.; Manada, C.; Rosing, H.; Stokvis, E.; Kettenes-van den Bosch, J. J.; Bult, A.; Beijnen, J. H.

CORPORATE SOURCE: Department of Pharmacy and Pharmacology, Slotervaart Hospital, The Netherlands Cancer Institute, Amsterdam,

1066 EC, Neth.
SOURCE: Journal of Liquid Chromatography & Related Technologies (2001), 24(20), 3141-3155
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Dec 2001
AB Kahalalide F is a cyclic depsipeptide derived from the marine mollusc Elysia rufescens, an organism living in the seas near Hawaii. On the basis of its in vitro and in vivo selectivity, kahalalide F is currently developed as a potential anticancer agent against androgen independent prostate tumors. The development and validation of a reversed-phase high performance liquid chromatog. (RP-HPLC) method with ultra-violet (UV) detection for the quantification and purity determination of kahalalide F in raw drug substance and pharmaceutical dosage form was described. Linear calibration curves in the range of 0.5-12.5 μg/mL of kahalalide F with correlation coeffs. > 0.999 were obtained. Within-run and between-run precisions were ≤ 3.0% and accuracy was within 100.4-103.2%. The assay proved selective, as determined by stress-testing, confirming its stability indicating capacity. Using liquid chromatog.-mass spectrometry (LC-MS) anal., kahalalide G, the hydrolyzed open-chain analog of kahalalide F, appeared upon heating and in acidic media. Furthermore, it was shown that kahalalide F remains its integrity in the freeze-dried pharmaceutical dosage form.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 27 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:849600 HCAPLUS Full-text
DOCUMENT NUMBER: 136:99533
TITLE: Chemical defenses of the sacoglossan mollusk Elysia rufescens and its host alga Bryopsis sp.
AUTHOR(S): Becerro, Mikel A.; Goetz, Gilles; Paul, Valerie J.; Scheuer, Paul J.
CORPORATE SOURCE: Department of Chemistry, University of Hawaii at Manoa, Honolulu, HI, 96822, USA
SOURCE: Journal of Chemical Ecology (2001), 27(11), 2287-2291
CODEN: JCECD8; ISSN: 0098-0331
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Nov 2001
AB Sacoglossans are a group of opisthobranch mollusks that have been the source of numerous secondary metabolites; however, there are few examples where a defensive ecol. role for these compds. has been demonstrated exptl. We investigated the deterrent properties of the sacoglossan Elysia rufescens and its food alga Bryopsis sp. against natural fish predators. Bryopsis sp. produces kahalalide F, a major depsipeptide that is accumulated by the sacoglossan and that shows in vitro cytotoxicity against several cancer cell lines. Our data show that both Bryopsis sp. and Elysia rufescens are chemical protected against fish predators, as indicated by the deterrent properties of their exts. at naturally occurring concns. Following bioassay-guided fractionation, we observed that the antipredatory compds. of Bryopsis sp. were present in the butanol and chloroform fractions, both containing the depsipeptide kahalalide F. Antipredatory compds. of Elysia rufescens were exclusively present in the dichloromethane fraction. Further bioassay-guided fractionation led to the isolation of kahalalide F as the only compound responsible for the deterrent properties of the sacoglossan. Our data show that kahalalide F protects both Bryopsis sp. and Elysia rufescens from fish

predation. This is the first report of a diet-derived depsipeptide used as a chemical defense in a sacoglossan.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 28 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:846704 HCAPLUS Full-text
DOCUMENT NUMBER: 137:98856
TITLE: Development of a lyophilized parenteral pharmaceutical formulation of the investigational polypeptide marine anticancer agent kahalalide F
AUTHOR(S): Nuijen, B.; Bouma, M.; Talsma, H.; Manada, C.; Jimeno, J. M.; Lopez-Lazaro, L.; Bult, A.; Beijnen, J. H.
CORPORATE SOURCE: Department of Pharmacy and Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, 1066 EC, Neth.
SOURCE: Drug Development and Industrial Pharmacy (2001), 27(8), 767-780
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Nov 2001
AB Kahalalide F is a novel antitumor agent isolated from the marine mollusk Elysia rufescens; it has shown highly selective in vitro activity against androgen-independent prostate tumors. The purpose of this study was to develop a stable parenteral formulation of kahalalide F to be used in early clin. trials. Solubility and stability of kahalalide F were studied as a function of polysorbate 80 (0.1%-0.5% w/v) and citric acid monohydrate (5-15 mM) concns. using an exptl. design approach. Stabilities of kahalalide F lyophilized products containing crystalline (mannitol) or amorphous (sucrose) bulking agents were studied at +5° and +30°±60% relative humidity (RH) in the dark. Lyophilized products were characterized by IR (IR) spectroscopy and differential scanning calorimetry (DSC). Recovery studies after reconstitution of kahalalide F lyophilized product and further dilution in infusion fluid were carried out to select an optimal reconstitution vehicle. It was found that a combination of polysorbate 80 and citric acid monohydrate is necessary to solubilize kahalalide F. Lyophilized products were considerably less stable with increasing polysorbate 80 and citric acid monohydrate concns., with polysorbate 80 being the major effector. A combination of 0.1% w/v polysorbate 80 and 5 mM citric acid monohydrate was selected for further investigation. Lyophilized products containing sucrose as a bulking agent were more stable compared to the products containing mannitol. The glass transition temperature of the sucrose-based product was determined to be +46°. The amorphous state of the product was confirmed by IR anal. A solution composed of Cremophor EL, ethanol, and water for injection (5%/5%/90% volume/volume/v CEW) kept kahalalide F in solution after reconstitution and further dilution with 0.9% w/v sodium chloride (normal saline) to 1.5 μg/m. A stable lyophilized formulation was presented containing 100 μg of kahalalide F, 100 mg sucrose, 2.1 mg citric acid monohydrate, and 2 mg polysorbate 80 to be reconstituted with a vehicle composed of 5%/5%/90% volume/volume/v CEW and to be diluted further using normal saline.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 29 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:781497 HCAPLUS Full-text
DOCUMENT NUMBER: 136:86050
TITLE: Synthesis and Structure Determination of Kahalalide F

AUTHOR(S): Lopez-Macia, Angel; Jimenez, Jose Carlos; Royo, Miriam; Giralt, Ernest; Albericio, Fernando
CORPORATE SOURCE: Department of Organic Chemistry, University of Barcelona, Barcelona, 08028, Spain
SOURCE: Journal of the American Chemical Society (2001), 123(46), 11398-11401
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:86050
ED Entered STN: 28 Oct 2001
AB Kahalalide F, the only member of the kahalalide peptide family with important bioactivity, is in clin. trials for treatment of prostate cancer. An efficient solid-phase synthetic approach is reported. Kahalalide F presents several synthetic difficulties: (i) an ester bond between two β-branched and sterically hindered amino acids; (ii) a didehydroamino acid; and (iii) a rather hydrophobic sequence with two fragments containing several β-branched amino acids in a row, one of them terminated with a saturated aliphatic acid. The cornerstones of our strategy were (i) a quasiorthogonal protecting system with allyl, tert-Bu, fluorenyl, and trityl-based groups, (ii) azabenzotriazole coupling reagents, (iii) formation of the didehydroamino acid residue on the solid phase, and (iv) cyclization and final purification in solution HPLC, high-field NMR, and biol. activity studies showed that the correct stereochem. of the natural product is that proposed by Rinehart et al., whereas the stereochem. proposed by Scheuer et al. is that of a biol. less active diastereoisomer.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 30 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:755009 HCAPLUS Full-text
DOCUMENT NUMBER: 136:79394
TITLE: Chemical and enzymatic stability of a cyclic depsipeptide, the novel, marine-derived, anti-cancer agent kahalalide F
AUTHOR(S): Sparidans, Rolf W.; Stokvis, Ellen; Jimeno, Jose M.; Lopez-Lazaro, Luis; Schellens, Jan H. M.; Beijnen, Jos H.
CORPORATE SOURCE: Faculty of Pharmacy, Department of Biomedical Analysis, Division of Drug Toxicology, Utrecht University, Utrecht, 3584 CA, Neth.
SOURCE: Anti-Cancer Drugs (2001), 12(7), 575-582
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 17 Oct 2001
AB Kahalalide F is a cyclic depsipeptide isolated from the Hawaiian mollusk Elysia rufescens. This compound is under present phase I clin. investigation as an anti-tumor drug. The role of possible metabolic reactions of this drug in (pre-)clin. investigations has not yet been explored. The first results for kahalalide F in this field of research are given in this paper. The chemical degradation of kahalalide F was investigated under acid, neutral and alkaline conditions using high-performance liquid chromatog. with UV detection. The half-lives at 80° were 1.1, 20 and 8.6 h at pH 0, 1 and 7, resp. At 26° and pH 11, the half-life was 1.65 h. At pH 7 and 11, only one reaction product of kahalalide F was observed, kahalalide G, the hydrolyzed lactone product of kahalalide F. At pH 0 and 1, addnl. reaction products emerged. Metabolic conversion of kahalalide F was tested in vitro using three

different enzyme systems based on pooled human microsomes, pooled human plasma and uridine 5'-diphosphoglucuronyl transferase, resp. The incubated samples were analyzed using the same chromatog. technique as for the degradation samples. Biotransformations were not observed under these conditions and, therefore, it is concluded that kahalalide F is a metabolically stable drug.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 31 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:706055 HCAPLUS Full-text
DOCUMENT NUMBER: 136:406817
TITLE: Compatibility and stability of the investigational polypeptide marine anticancer agent kahalalide F in infusion devices
AUTHOR(S): Nuijen, Bastiaan; Bouma, Marjan; Manada, Consuelo; Jimeno, Jose M.; Lazaro, Luis L.; Bult, Auke; Beijnen, Jos H.
CORPORATE SOURCE: Department of Pharmacy and Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, 1066 EC, Neth.
SOURCE: Investigational New Drugs (2001), 19(4), 273-281
CODEN: INNDDK; ISSN: 0167-6997
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 27 Sep 2001
AB Kahalalide F is a novel marine-derived antitumor agent isolated from the marine mollusk Elysia rufescens, an organism living in the seas near Hawaii. The compound has shown highly selective in vitro activity against prostate tumors and phase I trials in patients with androgen independent prostate tumors incorporating a daily times five and weekly schedule have been initiated. Kahalalide F is pharmaceutically formulated as a lyophilized product containing 150 μg active substance per dosage unit. Prior to i.v. administration it is reconstituted with a solution composed of Cremophor EL, ethanol absolute and Water for Injection (CEW, 5/5/90% volume/volume/v) with further dilution in 0.9% w/v sodium chloride for infusion. The aim of this study was to investigate the compatibility and stability of kahalalide F with different infusion systems prior to the start of clin. trials with the compound Due to the presence of Cremophor EL in the infusion solution, leaching of diethylhexyl phthalate (DEHP) from polyvinyl chloride infusion containers (PVC, Add-a-Flex) was found. Loss of kahalalide F as a consequence of sorption to contact surfaces was shown with an infusion container composed of low d. polyethylene (LD-PE, Miniflac). We conclude that kahalalide F must be administered in a 3-h infusion in concns. of 0.5 μg/mL to 14.7 μg/mL using an administration set consisting of a glass container and a low-extrables, DEHP-free extension set. Kahalalide F 150 μg/vial powder for infusion reconstituted with 5/5/90% volume/volume/v CEW is stable in the original container for at least 24 h at room temperature (+20-25°) and ambient light conditions. Infusion solns. stored in glass infusion containers at either room temperature (+20-25°, in the dark) or refrigerated conditions (+2-8°, in the dark) are stable for at least 5 days after preparation
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 32 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:598019 HCAPLUS Full-text
DOCUMENT NUMBER: 135:167039
TITLE: Preparation of kahalalide compounds

INVENTOR(S): Albericio, Fernando; Giralt, Ernest; Jimenez, Jose Carlos; Lopez, Angel; Manzanares, Ignacio; Rodrigues, Ignacio; Royo, Miriam
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2001058934	A2	20010816	WO 2001-GB576		20010209	<--
WO 2001058934	A3	20020321				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW						
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
CA 2399187	A1	20010816	CA 2001-2399187		20010209	<--
EP 1254162	A2	20021106	EP 2001-904169		20010209	<--
EP 1254162	B1	20070829				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR						
BR 2001008213	A	20030305	BR 2001-8213		20010209	<--
JP 2003522198	T	20030722	JP 2001-558081		20010209	<--
HU 200301817	A2	20030929	HU 2003-1817		20010209	<--
NZ 520488	A	20050324	NZ 2001-520488		20010209	<--
AU 783542	B2	20051110	AU 2001-32086		20010209	<--
RU 2280039	C2	20060720	RU 2002-123877		20010209	<--
NO 2002003749	A	20021007	NO 2002-3749		20020808	<--
MX 2002PA07760	A	20021023	MX 2002-PA7760		20020809	<--
BG 107020	A	20030530	BG 2002-107020		20020821	<--
US 2004214755	A1	20041028	US 2003-182881		20030603	<--
PRIORITY APPLN. INFO.:			GB 2000-2952	A	20000209	<--
			WO 2001-GB576	W	20010209	<--

OTHER SOURCE(S): MARPAT 135:167039
ED Entered STN: 17 Aug 2001
AB Kahalalide F and kahalalide mimic compds. having useful biol. activity were prepared The mimics differ from natural kahalalides in one or more of the following respects: at least one amino acid which is not the same as an amino acid present in the parent compound and at least one methylene group or substituent in the side chain acyl group of the parent compound is addnl. or omitted. Approx. 40 kahalalide analogs, including 5-MeHex-D-Val-Thr-Val-D-Val-D-Pro-Orn-D-allo-Ile-cyclo(D-allo-Thr-D-allo- Ile-D-Val-Phe-Etg-Val) (5-MeHex is 5-methylhexanoyl and Etg is ethylglycine residue), were prepared by the solid phase method and their cytotoxicities (IC50 values) tabulated.

L10 ANSWER 33 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:593276 HCAPLUS Full-text
DOCUMENT NUMBER: 135:170762
TITLE: Cytotoxic and antimicrobial activities of Kahalalide F from Elysia rufescens
INVENTOR(S): Scheuer, Paul J.; Hamann, Mark T.; Gravalos, Dolores

G.
PATENT ASSIGNEE(S): PharmaMar, S.A., Spain
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6274551	B1	20010814	US 1994-192569	19940203 <--
US 6011010	A	20000104	US 1997-935073	19970925 <--
US 39496	E1	20070227	US 2003-642006	20030814 <--
PRIORITY APPLN. INFO.:			GB 1993-2046 A	19930203 <--
			US 1994-192569 A1	19940203 <--

ED Entered STN: 16 Aug 2001
AB Kahalalide F (I) is isolated from a sacoglossan (Elysia rufescens). I may be used in the manufacture of pharmaceutical compns. or in the treatment of tumors or viral conditions. Two hundred sacoglossans (E. rufescens), were collected and extracted 3 times with EtOH. The combined exts. were then chromatographed on silica gel flash chromatog. by using hexane, hexane/EtOAc (1:1), EtOAc, EtOAc/MeOH (1:1), MeOH, MeOH/HOAc (98:2). The depsipeptides were found in the EtOAc/MeOH (1:1) fraction. Repeated RP-HPLC yielded 6 new depsipeptides, out of which I was isolated and its structure was determined
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 34 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:128631 HCAPLUS Full-text
DOCUMENT NUMBER: 132:290934
TITLE: Marine natural products as antituberculosis agents
AUTHOR(S): El Sayed, Khalid A.; Bartyzel, Piotr; Shen, Xiaoyu; Perry, Tony L.; Zjawiony, Jordan K.; Hamann, Mark T.
CORPORATE SOURCE: Department of Pharmacognosy, NCNPR School of Pharmacy, The University of Mississippi, MS, 38677, USA
SOURCE: Tetrahedron (2000), 56(7), 949-953
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 25 Feb 2000
AB In an attempt to characterize addnl. structural classes that could serve as lead antituberculosis agents, 48 structurally diverse marine-derived natural and semisynthetic compds. were examined for in vitro activity against Mycobacterium tuberculosis. Three new classes of compds. including C-19 hydroxy steroids [e.g. litosterol (I)], scalarin sesquiterpenoids [e.g. heteronemin (II)], and tetrabromo spirocyclohexadienylisoxazolines [e.g. 11-hydroxyaerothionin (III)] have been identified as having potential as leads for continued investigations as new antituberculosis agents. New addns. to the established antituberculosis structural classes quinone-methide and peptide are also reported.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 35 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:10614 HCAPLUS Full-text
DOCUMENT NUMBER: 132:59154
TITLE: Kahalalide F or salts of this sacoglossan peptide in treatment of tumors and

viral infections in mammals
INVENTOR(S): Scheuer, Paul J.; Hamann, Mark T.; Gravalos, Dolores G.
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain
SOURCE: U.S., 5 pp., Cont. of U.S. Ser. No. 192,569.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6011010	A	20000104	US 1997-935073	19970925 <--
US 6274551	B1	20010814	US 1994-192569	19940203 <--
PRIORITY APPLN. INFO.:			US 1994-192569	A1 19940203 <--

ED Entered STN: 06 Jan 2000
AB Kahalalide F, a peptide that may be isolated from a sacoglossan (Elysia rufescens), or a pharmaceutically acceptable salt thereof, may be used in the treatment of mammalian tumors or viral infections. Use for treatment of human lung carcinoma, human colon carcinoma, Herpes simplex and Vesicular Stomatitis viral infections in mammals is claimed.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 36 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:631977 HCAPLUS Full-text
DOCUMENT NUMBER: 131:337344
TITLE: The absolute stereochemistry of kahalalide F. [Erratum to document cited in CA131:157974]
AUTHOR(S): Goetz, Gilles; Yoshida, Wesley Y.; Scheuer, Paul J.
CORPORATE SOURCE: Department of Chemistry, University of Hawaii, Honolulu, HI, 96822, USA
SOURCE: Tetrahedron (1999), 55(40), 11957
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Oct 1999
AB On page vii, in the graphical abstract, L-Pro should read D-Pro.

L10 ANSWER 37 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:392419 HCAPLUS Full-text
DOCUMENT NUMBER: 131:157974
TITLE: The absolute stereochemistry of kahalalide F
AUTHOR(S): Goetz, Gilles; Yoshida, Wesley Y.; Scheuer, Paul J.
CORPORATE SOURCE: Dep. Chemistry, Univ. Hawaii, Honolulu, HI, 96822, USA
SOURCE: Tetrahedron (1999), 55(25), 7739-7746
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Jun 1999
AB Kahalalide F(1) is a depsipeptide of 14 residues, five of which form a 19-membered ring. It was isolated from a marine mollusk, Elysia rufescens, and is currently in preclin. trails against lung and colon cancers. It was known from conventional amino acid anal. that five valine and two threonine residues represented D- and L-enantiomers, but their position in the mol. was not

known. After extensive hydrolytic trials, a combination of acid hydrolysis and hydrazinolysis succeeded in definitive stereochem. assignment.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 38 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:447351 HCAPLUS Full-text
DOCUMENT NUMBER: 129:228328
TITLE: Kahalalides: Bioactive Peptides from a Marine Mollusk Elysia rufescens and Its Algal Diet Bryopsis sp.. [Erratum to document cited in CA125:190997]
AUTHOR(S): Hamman, Mark T.; Otto, Clifton S.; Scheuer, Paul J.; Dunbar, D. Chuck
CORPORATE SOURCE: Department of Chemistry, University of Hawaii of Manoa, Honolulu, HI, 96822, USA
SOURCE: Journal of Organic Chemistry (1998), 63(14), 4856
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 20 Jul 1998
AB On page 6595, the labeled amino acid on the structure of kahalalide F (6) should read D-Pro rather than L-Pro..

L10 ANSWER 39 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:531764 HCAPLUS Full-text
DOCUMENT NUMBER: 125:190997
TITLE: Kahalalides: bioactive peptides from a marine mollusk Elysia rufescens and its algal diet Bryopsis sp.
AUTHOR(S): Hamann, Mark T.; Otto, Clifton S.; Scheuer, Paul J.; Dunbar, D. Chuck
CORPORATE SOURCE: Department of Chemistry, University of Hawaii of Manoa, Honolulu, HI, 96822, USA
SOURCE: Journal of Organic Chemistry (1996), 61(19), 6594-6600
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Sep 1996
AB In addition to the previously reported bioactive kahalalide F, 6 new peptides are described. Six of these, including kahalalide F, are cyclic depsipeptides, ranging from a C31 tripeptide to a C75 tridecapeptide isolated from a sacoglossan mollusk, E. rufescens. The mollusk feeds on a green alga, Bryopsis sp., which has also been shown to elaborate some of these peptides in smaller yields, in addition to an acyclic analog of F, kahalalide G. The bioassay results of antitumor, antiviral, antimalarial, and OI (activity against AIDS opportunistic infections) tests are reported.

L10 ANSWER 40 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:423809 HCAPLUS Full-text
DOCUMENT NUMBER: 125:131710
TITLE: The marine environment: A resource for prototype antimalarial agents
AUTHOR(S): El Sayed, Khalid A.; Dunbar, D. Charles; Goins, D.

Keith; Cordova, Cindy R.; Perry, Tony L.; Wesson, Keena J.; Sanders, Sharon C.; Janus, Scott A.; Hamann, Mark T.
CORPORATE SOURCE: Center the Development Natural Products, University Mississippi, University, MS, 38677, USA
SOURCE: Journal of Natural Toxins (1996), 5(2), 261-285
CODEN: JNTOER; ISSN: 1058-8108
PUBLISHER: Alaken
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Jul 1996
AB In an attempt to characterize addnl. structural classes that could serve as prototype antimalarial agents, 28 structurally diverse marine compds. were examined for in vitro activity against the D6 and W2 clones of Plasmodium falciparum. Several new classes of compds. have been identified as having potential as prototypes for the development of new antimalarial agents.

L10 ANSWER 41 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:58580 HCAPLUS Full-text
DOCUMENT NUMBER: 124:164539
TITLE: The antitumoral compound Kahalalide F acts on cell lysosomes
AUTHOR(S): Garcia-Rocha, Mar; Bonay, Pedro; Avila, Jesus
CORPORATE SOURCE: 28049-Madrid, Spain
SOURCE: Cancer Letters (Shannon, Ireland) (1996), 99(1), 43-50
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Jan 1996
AB The target for the antitumoral peptidic drug, Kahalalide F, has been studied in cultured cells. In the presence of the compound, the cells became impressively swollen, showing the formation of large vacuoles. The formation of these vacuoles appears to be the consequence of changes in lysosomal membranes. Thus, lysosomes are a target for Kahalalide F action.

L10 ANSWER 42 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:130565 HCAPLUS Full-text
DOCUMENT NUMBER: 122:17167
TITLE: Kalahide F as cytotoxic and antiviral and antifungal compound
INVENTOR(S): Schauer, Paul J.; Hamann, Mark T.; Gravalos, Dolores G.
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 610078	A1	19940810	EP 1994-300780	19940202 <--
EP 610078	B1	19970416		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

AT 151776	T	19970515	AT 1994-300780	19940202 <--
ES 2102772	T3	19970801	ES 1994-300780	19940202 <--
CA 2114859	A1	19940804	CA 1994-2114859	19940203 <--
AU 9454911	A	19940811	AU 1994-54911	19940203 <--
AU 677258	B2	19970417		
ZA 9400748	A	19940929	ZA 1994-748	19940203 <--
JP 07070185	A	19950314	JP 1994-43024	19940203 <--
JP 3452628	B2	20030929		

PRIORITY APPLN. INFO.: GB 1993-2046 A 19930203 <--
ED Entered STN: 08 Nov 1994
AB Kalahide F (I) which is isolated from sacoglossan may be used in the treatment of tumors or viral conditions. I was isolated from Elysia rufescens by extraction and silica gel flash chromatog. The antifungal, antiviral and cytotoxicity activity of I is shown.

L10 ANSWER 43 OF 56 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:491602 HCAPLUS Full-text
DOCUMENT NUMBER: 119:91602
TITLE: Kahalalide F: a bioactive depsipeptide from the sacoglossan mollusk Elysia rufescens and the green alga Bryopsis sp
AUTHOR(S): Hamann, Mark T.; Scheuer, Paul J.
CORPORATE SOURCE: Dep. Chem., Univ. Hawaii, Honolulu, HI, 96822, USA
SOURCE: Journal of the American Chemical Society (1993), 115(13), 5825-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Sep 1993
AB Kahalalide F, C75H124N14O16, was isolated from a sacoglossan mollusk Elysia rufescens and its food source, a green alga, Bryopsis. Its structure was determined by spectral detns. and chiral amino acid anal.

L10 ANSWER 44 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2007:135061 USPATFULL Full-text
TITLE: New antitumoral compounds
INVENTOR(S): Palomera, Fernando Albericio, Barcelona, SPAIN
Donis, Ariadna Fernandez, Barcelona, SPAIN
Lledo, Ernest Giralt, Barcelona, SPAIN
Cantador, Carolina Gracia, Barcelona, SPAIN
Rodriguez, Pilar Lopez, Barcelona, SPAIN
Colomer, Sonia Varon, Barcelona, SPAIN
Marchante, Carmen Cuevas, Madrid, SPAIN
Macia, Angel Lopez, Madrid, SPAIN
Solloso, Andres Francesch, Madrid, SPAIN
Garcia, Jose-Carlos Jimenez, Barcelona, SPAIN
Exposito, Miriam Royo, Barcelona, SPAIN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007117743	A1	20070524	
APPLICATION INFO.:	US 2004-570734	A1	20040909	(10)
	WO 2004-GB3847		20040909	
			20061018	PCT 371 date

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 2003-21066	20030909	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KING & SPALDING, 1185 AVENUE OF THE AMERICAS, NEW YORK, NY, 10036-4003, US
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 2871
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New analogues of kahalalide F are provided.

L10 ANSWER 45 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2007:50754 USPATFULL Full-text
TITLE: Kahalalide F and compositions and uses thereof
INVENTOR(S): Scheuer, Alice E. D., Honolulu, HI, UNITED STATES
legal representative
Hamann, Mark T., Oxford, MS, UNITED STATES
Gravalos, Dolores G., Madrid, SPAIN
Scheuer, Paul J., United States deceased
Scheuer, Paul J., Honolulu, HI, UNITED STATES
PATENT ASSIGNEE(S): PharmaMar, S.A., Madrid, SPAIN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 39496	E1	20070227	
	US 6274551		20010814	(Original)<--
APPLICATION INFO.:	US 2003-642006		20030814	(10) <--
	US 1994-192569		19940203	(Original)<--

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1993-2046	19930203 <--

DOCUMENT TYPE: Reissue
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wessendorf, T. D.
LEGAL REPRESENTATIVE: Morgan & Finnegan, L.L.P., Sonnenfeld, Kenneth H., Willis, Michael A.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 5
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 456
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB (Kalahide) Kahalalide F, of formula I below, may be isolated from a sacoglossan. The compound may be used in the manufacture of pharmaceutical compositions or in the treatment of tumors or viral conditions ##STR1##

L10 ANSWER 46 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2007:36872 USPATFULL Full-text
TITLE: Use of Kahalalide Compounds for the Manufacture of a Medicament for the Treatment of Psoriasis
INVENTOR(S): Izquierdo Delso, Miguel Angel, Madrid, SPAIN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007032412	A1	20070208	
APPLICATION INFO.:	US 2004-546758	A1	20040226	(10)
	WO 2004-GB757		20040226	
			20061010	PCT 371 date

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 2003-4367	20030226	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KING & SPALDING, 1185 AVENUE OF THE AMERICAS, NEW YORK, NY, 10036-4003, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 481
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Kahalalide compounds, in particular kahalalide F, are of use in a method to treat a mammal suffering from skin disease with avoiding toxicity and leading to clinical improvement.

L10 ANSWER 47 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2006:275123 USPATFULL Full-text
TITLE: New antitumoral compounds
INVENTOR(S): Faircloth, Glynn Thomas, Cambridge, MA, UNITED STATES
Marchante, Maria Del Carmen Cuevas, Madrid, SPAIN

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2006234920	A1	20061019		
APPLICATION INFO.:	US 2003-531533	A1	20031020	(10)	<--
	WO 2003-US33207		20031020		<--
			20060425	PCT 371 date	

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 2003-4367	20030226	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORGAN & FINNEGAN, L.L.P., 3 WORLD FINANCIAL CENTER, NEW YORK, NY, 10281-2101, US
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 777
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to new kahalalide antitumoral compounds, in particular to analogues of kahalalide F, useful as antitumoral, antiviral, antifungal agents and in the treatment of psoriasis.

L10 ANSWER 48 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2006:27536 USPATFULL Full-text
TITLE: Novel dosage form
INVENTOR(S): Vaya, Navin, Gujarat, INDIA
Karan, Rajesh Singh, Gujarat, INDIA
Sadanand, Sunil, Gujarat, INDIA
Gupta, Vinod Kumar, Gujarat, INDIA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006024365	A1	20060202	
APPLICATION INFO.:	US 2005-134633	A1	20050519	(11)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-630446, filed on 29 Jul 2003, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	IN 2002-6992002	20020805	<--
	IN 2002-6972002	20020805	<--
	IN 2003-802003	20030122	<--
	IN 2003-822003	20030122	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HEDMAN & COSTIGAN P.C., 1185 AVENUE OF THE AMERICAS, NEW YORK, NY, 10036, US
NUMBER OF CLAIMS: 65
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 3850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form.

L10 ANSWER 49 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2005:171786 USPATFULL Full-text
TITLE: IAP nucleobase oligomers and oligomeric complexes and uses thereof
INVENTOR(S): LaCasse, Eric, Ottawa, CANADA
McManus, Daniel, Ottawa, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005148535	A1	20050707	
APPLICATION INFO.:	US 2004-975974	A1	20041028	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-516192P	20031030 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110, US
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 3022
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides nucleobase oligomers and oligomer complexes that inhibit expression of an IAP polypeptide, and methods for using them to induce apoptosis in a cell. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compositions. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent.

L10 ANSWER 50 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2005:138567 USPATFULL Full-text
TITLE: Methods and reagents for the treatment of proliferative diseases

INVENTOR(S): LaCasse, Eric, Ottawa, CANADA
McManus, Daniel, Ottawa, CANADA
Durkin, Jon P., Montreal, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005119217	A1	20050602	
APPLICATION INFO.:	US 2004-975790	A1	20041028	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-516263P	20031030 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110, US
NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 5896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention features methods, compositions, and kits for treating a patient having a proliferative disease.

L10 ANSWER 51 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2005:63515 USPATFULL Full-text
TITLE: Kahalalide compounds for use in cancer therapy
INVENTOR(S): Jimeno, Jose, Madrid, SPAIN
Lazaro, Luis Lopez, Madrid, SPAIN
Casado, Ana Ruiz, Madrid, SPAIN
Izquierdo, Miguel Angel, Madrid, SPAIN
Trigo, Jose Manuel, Malaga, SPAIN
Schellens, Jan, Kockengen, NETHERLANDS
Paz-Ares, Luis, Madrid, SPAIN

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2005054555	A1	20050310		
APPLICATION INFO.:	US 2004-492670	A1	20041103	(10)	<--
	WO 2002-GB4735		20021018		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-348449P	20011019 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110
NUMBER OF CLAIMS: 47
EXEMPLARY CLAIM: 1
LINE COUNT: 850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Procedures for clinical trials of kahalalide compounds are provided, leading to new formulations of kahalalide compounds.

L10 ANSWER 52 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2004:274253 USPATFULL Full-text

TITLE: Kahalalide f and related compounds
INVENTOR(S): Albericio, Fernando, Barcelona, SPAIN
Giralt, Ernest, Barcelona, SPAIN
Jimenez, Jose Carlos, Barcelona, SPAIN
Lopez, Angel, Barcelona, SPAIN
Manzanares, Ignacio, Madrid, SPAIN
Rodrigues, Ignacio, Madrid, SPAIN
Royo, Miriam, Barcelona, SPAIN

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2004214755	A1	20041028		
APPLICATION INFO.:	US 2003-182881	A1	20030603	(10)	<--
	WO 2001-GB576		20010209		<--

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 2000-2952	20000209	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 1691
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process is provided for preparing kahalalide F and which leads to other kahalalide mimic compounds having useful biological activity.

L10 ANSWER 53 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2004:121167 USPATFULL Full-text
TITLE: Treatment for inhibiting neoplastic lesions
INVENTOR(S): Shanahan-Prendergast, Elizabeth, County Kildare, IRELAND

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2004092583	A1	20040513		
APPLICATION INFO.:	US 2004-250535	A1	20040102	(10)	<--
	WO 2002-IE1		20020102		

	NUMBER	DATE	
PRIORITY INFORMATION:	IE 2001-20010002	20010102	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HOFFMANN & BARON, LLP, 6900 JERICHO TURNPIKE, SYOSSET, NY, 11791
NUMBER OF CLAIMS: 69
EXEMPLARY CLAIM: 1
LINE COUNT: 2329
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention discloses the use of incensole and/or furanogermacrens, derivatives metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compounds can be administered alone or in combination with conventional chemotherapeutic, anti-rival, anti-parasite agents, radiation and/or surgery.

L10 ANSWER 54 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2004:88919 USPATFULL Full-text
TITLE: Kahalalide f formulation
INVENTOR(S): Faircloth, Glynn Thomas, Avenue Cambridge, MA, UNITED STATES
Nuyen, Bastian, Amsterdam, NETHERLANDS
Weitman, Steve, San Antonio, TX, UNITED STATES

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2004067895	A1	20040408		
APPLICATION INFO.:	US 2003-399571	A1	20031114	(10)	<--
	WO 2001-GB4821		20011031		<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 392
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New formulations and new uses of kahalalide F are provided.

L10 ANSWER 55 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2001:131266 USPATFULL Full-text
TITLE: Cytotoxic and antiviral compound
INVENTOR(S): Scheuer, Paul J, Honolulu, HI, United States
Hamann, Mark T, Honolulu, HI, United States
Gravalos, Dolores G., Madrid, Spain
PATENT ASSIGNEE(S): PharmaMar, S.A., Madrid, Spain (non-U.S. corporation)

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 6274551	B1	20010814		<--
APPLICATION INFO.:	US 1994-192569		19940203	(8)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: MacMillan, Keith D.
ASSISTANT EXAMINER: Wessendorf, T. D.
LEGAL REPRESENTATIVE: Linek, Ernest V.Banner & Witcoff, Ltd.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 425
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Kalahide F, of formula I below, may be isolated from a sacoglossan. The compound may be used in the manufacture of pharmaceutical compositions or in the treatment of tumors or viral conditions. ##STR1##

L10 ANSWER 56 OF 56 USPATFULL on STN
ACCESSION NUMBER: 2000:1853 USPATFULL Full-text
TITLE: Cytotoxic and antiviral compound
INVENTOR(S): Scheuer, Paul J, Honolulu, HI, United States
Hamann, Mark T, Honolulu, HI, United States
Gravalos, Dolores G., Madrid, Spain
PATENT ASSIGNEE(S): Pharma Mar, s.a., Madrid, Spain (non-U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION:	US 6011010	20000104	<--
APPLICATION INFO.:	US 1997-935073	19970925 (8)	<--
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-192569, filed on 3 Feb 1994		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	MacMillan, Keith D.		
ASSISTANT EXAMINER:	Wessendorf, T. D.		
LEGAL REPRESENTATIVE:	Linek, Ernest V.Banner & Witcoff, Ltd.		
NUMBER OF CLAIMS:	4		
EXEMPLARY CLAIM:	1		
LINE COUNT:	266		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Kalahide F. of formula I below, may be isolated from a secoglossan. The compound may be used in the manufacture of pharmaceutical compositions or in the treatment of tumors or viral conditions. ##STR1##

Inventor search history

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=> d his L7

     (FILE 'HCAPLUS, USPATFULL' ENTERED AT 09:17:18 ON 04 SEP 2007)
L7           64 S L5 OR L6

=> d que L7
L5           64 SEA ("FAIRCLOTH GLYNN"/AU OR "FAIRCLOTH GLYNN T"/AU OR
                "FAIRCLOTH GLYNN T JR"/AU OR "FAIRCLOTH GLYNN THOMAS"/AU)
L6            1 SEA "MARCHANTE MARIA DEL CARMEN CUEVAS"/AU
L7           64 SEA L5 OR L6
```

Subsequence search results

```
=> d L7 1-36 ibib ab

L7   ANSWER 1 OF 64  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:1043879  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:159
TITLE:                    Development of a liquid chromatography/tandem mass
                          spectrometry assay for the quantification of PM02734,
                          a novel antineoplastic agent, in dog plasma
AUTHOR(S):                Yin, Jianming; Aviles, Pablo; Lee, William; Ly, Carl;
                          Guillen, Maria Jose; Munt, Simon; Cuevas, Carmen;
                          Faircloth, Glynn
CORPORATE SOURCE:         PharmaMar USA, Inc., Cambridge, MA, 02139-4616, USA
SOURCE:                   Rapid Communications in Mass Spectrometry (2006),
                          20(18), 2735-2740
                          CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER:                John Wiley & Sons Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A rapid and sensitive liquid chromatog./tandem mass spectrometry (LC/MS/MS)
     assay was developed and validated to quantify a novel antineoplastic agent,
     PM02734, in dog plasma. The method was validated to demonstrate the
     specificity, limit of quantification (LOQ), accuracy, and precision of
     measurements. The calibration range for PM02734 was established using PM02734
     stds. from 0.05 to 100 ng/mL in blank plasma. The dominating ions were doubly
     charged mol. ions [M+2H]2+ at m/z 740.0 instead of singly charged ones at m/z
     1478.4. The selected reaction monitoring (SRM), based on the m/z 740.0→212.2
     transition, was specific for PM02734, and that based on the m/z 743.8→212.2
     transition was specific for deuterated PM02734 (the internal standard, IS); no
     endogenous materials interfered with the anal. of PM02734 and IS from blank
     plasma. The assay was linear over the concentration range 0.05-100 ng/mL. In
     terms of sensitivity of assay 0.05 ng/mL is a very low LLOQ, especially
     considering PM02734 is a peptide. The correlation coeffs. for the calibration
     curves ranged from 0.9990 to 0.9999. The mean intraday and interday
     accuracies for all calibration stds. (n = 9) ranged from 93 to 111% (≤11%
     bias) in dog plasma, and the mean interday precision for all calibration stds.
     was less than 6.4%. The mean intra- and interday assay accuracy for all
     quality control replicates in dog plasma (n = 9), determined at each QC level
     throughout the validated runs, ranged from 85-111% (≤15% bias) and from 99-
     109% (≤9% bias), resp. The mean intra- and interday assay precision was less
     than 12.1 and 13.3% for all QC levels, resp. The assay has been used to
     support preclin. pharmacokinetic (PK) and toxicokinetic studies. The results
     showed that preclin. samples could be monitored for PM02734 up to 168 h after
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dosing, which allowed us to identify multiple elimination phases and accurately estimate PK information.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:487280 HCAPLUS Full-text
DOCUMENT NUMBER: 145:369384
TITLE: Induction of resistance to Aplidin in a human ovarian cancer cell line related to MDR expression
AUTHOR(S): Tognon, Gianluca; Bernasconi, Sergio; Celli, Nicola; Faircloth, Glynn T.; Cuevas, Carmen; Jimeno, Jose; Erba, Eugenio; D'Incalci, Maurizio
CORPORATE SOURCE: Department of Oncology, Flow Cytometry Unit, Mario Negri Institute, Milan, Italy
SOURCE: Cancer Biology & Therapy (2005), 4(12), 1325-1330
CODEN: CBTAAO; ISSN: 1538-4047
PUBLISHER: Landes Bioscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aplidin-resistant IGROV-1/APL cells were derived from the human ovarian cancer IGROV-1 cell line by exposing the cells to increasing concentration of Aplidin for eight months, starting from a concentration of 10 nM to a final concentration of 4 μM. IGROV-1/APL cell line possesses five fold relative resistance to Aplidin. IGROV-1/APL resistant cell line shows the typical MDR phenotype: (1) increased expression of membrane-associated P-glycoprotein, (2) cross-resistance to drugs like etoposide, doxorubicin, vinblastine, vincristine, taxol, colchicine and the novel anticancer drug Yondelis (ET-743). The Pgp inhibitor cyclosporin-A restored the sensitivity of IGROV-1/APL cells to Aplidin by increasing the drug intracellular concentration The resistance to Aplidin was not due to the other proteins, such as LPR-1 and MRP-1, being expressed at the same level in resistant and parental cell line. The finding that cells over-expressing Pgp are resistant to Aplidin was confirmed in CEM/VLB 100 cells, that was found to be 5-fold resistant to Aplidin compared to the CEM parental cell line.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:319213 HCAPLUS Full-text
DOCUMENT NUMBER: 144:343581
TITLE: Ecteinascidin compounds as anti-inflammatory agents
INVENTOR(S): Allavena, Paola; D'Incalci, Maurizio; Faircloth, Glynn Thomas
PATENT ASSIGNEE(S): Pharma Mar S.A., Sociedad Unipersonal, Spain; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006035244	A2	20060406	WO 2005-GB50164	20050928
WO 2006035244	A3	20060831		
WO 2006035244	A9	20070301		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005288696	A1	20060406	AU 2005-288696	20050928
CA 2583464	A1	20060406	CA 2005-2583464	20050928
EP 1812114	A2	20070801	EP 2005-805089	20050928

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

PRIORITY APPLN. INFO.:	US 2004-614093P	P	20040928
	WO 2005-GB50164	W	20050928

OTHER SOURCE(S): MARPAT 144:343581

AB The anti-inflammatory activity of ecteinascidin compds. was determined Ecteinascidin 743 (I) and other ecteinascidin compds. affect viability and functions of monocyte/macophages. Examples include noncytotoxic concs. of I inhibit in vitro and in vivo macrophage differentiation, I shows selective cytotoxic effect on mononuclear phagocytes, I inhibits the production of inflammatory cytokines/chemokines, and I was compared with antineoplastic agents currently used in ovarian cancer.

L7 ANSWER 4 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2006:203200 HCAPLUS Full-text
DOCUMENT NUMBER:	144:425023
TITLE:	Quantitative analysis of Variolin analog (PM01218) in mouse and rat plasma by high-performance liquid chromatography/electrospray ionization tandem mass spectrometry
AUTHOR(S):	Yin, Jianming; Aviles, Pablo; Ly, Carl; Lee, William; Guillen, Maria Jose; Munt, Simon; Cuevas, Carmen; Faircloth, Glynn
CORPORATE SOURCE:	PharmaMar USA Inc., Cambridge, MA, 02139-4616, USA
SOURCE:	Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2006), 832(2), 268-273 CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER:	Elsevier B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB PM01218 is a novel marine-derived alkaloid and has shown potent growth inhibitory activity against several human cancer cell lines. A rapid and sensitive high performance liquid chromatog./tandem mass spectrometry (HPLC-MS/MS) method was developed and validated to quantify PM01218 in mouse and rat plasma. The lower limit of quantitation (LLOQ) was 0.05 ng/mL. The calibration curve was linear from 0.05 to 100 ng/mL (R2 > 0.999). The assay was specifically based on the multiple reaction monitoring (MRM) transitions at m/z 278.4→184.2, no endogenous material interfaced with the anal. of PM01218 and its internal standard from blank mouse and rat plasma. The mean intra- and inter-day assay accuracy remained below 15 and 8%, resp., for all calibration stds. and QC samples. The intra- and inter-day assay precision was less than 12.8 and 8.5% for all QC levels, resp. The utility of the assay was demonstrated by pharmacokinetics studies of i.v. (bolus) PM01218 on SD rats.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1321640 HCAPLUS Full-text
DOCUMENT NUMBER: 145:116379
TITLE: Ecteinascidin 743 (ET-743; Yondelis), aplidin, and kahalide F
AUTHOR(S): Henriquez, Ruben; Faircloth, Glynn; Cuevas, Carmen
CORPORATE SOURCE: PharmaMar, Madrid, 28770, Spain
SOURCE: Anticancer Agents from Natural Products (2005), 215-240, 2 plates. Editor(s): Cragg, Gordon M.; Kingston, David G. I.; Newman, David J. CRC Press LLC: Boca Raton, Fla.
CODEN: 69HQQY; ISBN: 0-8493-1863-7
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review on the first generation of drugs isolated from marine organisms, i.e., Ecteinascidin 743, Aplidin, and Kahalide F. Topics discussed include their origin, mechanisms of action, chemical synthesis, drug development, and clin. studies.
REFERENCE COUNT: 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:730756 HCAPLUS Full-text
DOCUMENT NUMBER: 143:278611
TITLE: Combination of trabectedin and irinotecan is highly effective in a human rhabdomyosarcoma xenograft
AUTHOR(S): Riccardi, Anna; Meco, Daniela; Ubezio, Paolo; Mazzarella, Giorgio; Marabese, Mirko; Faircloth, Glynn T.; Jimeno, Jose; D'Incalci, Maurizio; Riccardi, Riccardo
CORPORATE SOURCE: Department of Pediatric Oncology, Catholic University, Rome, Italy
SOURCE: Anti-Cancer Drugs (2005), 16(8), 811-815
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our objective was to evaluate in vitro and in vivo the effect of the combination of trabectedin (Yondelis, ET-743) and irinotecan (CPT-11) or its major metabolite SN-38 in a human rhabdomyosarcoma cell line. The schedule trabectedin (1 h) followed by irinotecan or SN-38 (24 h) and the opposite sequence (irinotecan or SN-38 24 h followed by trabectedin 1 h) were analyzed in a rhabdomyosarcoma cell line. In vivo studies were conducted with trabectedin and irinotecan at the doses of 0.2 and 20 mg/kg, resp., simultaneously administered with a q4d + 3 schedule. In vitro studies indicated an overall additive effect [combination index (CI) relatively close to 1.0], with the former schedule slightly superior to the latter (at the IC50 effect levels: CI = 0.89 vs. 1.07). Neither transcription nor expression of DNA topoisomerase I was affected by trabectedin treatment. In vivo the therapeutic results of the combination were certainly more impressive: trabectedin and irinotecan combination caused a strong and long-lasting effect on tumor growth (tumor volume inhibition = 89%, log10 cell kill = 1.6), whereas each drug given as a single agent was only marginally active. The discrepancy between the in vitro and in vivo results suggests possible mechanisms involving host cells, other than tumor cells. The striking effects of the combination observed in vivo could be related to a combination of a

direct cytotoxic and an anti-inflammatory indirect effect. The very marked and long-lasting effect of the trabectedin and irinotecan combination in vivo suggests a basis for a clin. evaluation in pediatric patients with rhabdomyosarcoma.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:218200 HCAPLUS Full-text
DOCUMENT NUMBER: 142:430441
TITLE: Development of a liquid chromatography/tandem mass spectrometry assay for the quantification of PM00104, a novel antineoplastic agent, in mouse, rat, dog, and human plasma
AUTHOR(S): Yin, Jianming; Aviles, Pablo; Lee, William; Ly, Carl; Guillen, Maria Jose; Munt, Simon; Cuevas, Carmen; Faircloth, Glynn
CORPORATE SOURCE: PharmaMar USA, Inc., Cambridge, MA, 02139-4616, USA
SOURCE: Rapid Communications in Mass Spectrometry (2005), 19(5), 689-695
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid and sensitive liquid chromatog./tandem mass spectrometry (LC/MS/MS) assay was developed and validated to quantify a novel antineoplastic agent, PM00104, in mouse, rat, dog, and human plasma. The method was validated to demonstrate the specificity, limit of quantification (LOQ), accuracy, and precision of measurements. The calibration range for PM00104 was established using PM00104 stds. from 0.01-5.0 ng/mL in blank plasma. The selected reaction monitoring (SRM), based on the m/z 692.2 → 218.2 transition, was specific for PM00104, and that based on the m/z 697.2 → 218.2 transition was specific for PM00104 (13C2,2H3) (the internal standard, IS); no endogenous materials interfered with the anal. of PM00104 and IS from blank plasma. The assay was linear over the concentration range 0.01-5.0 ng/mL. The correlation coeffs. for the calibration curves ranged from 0.9981-0.9999. The mean intra-day and inter-day accuracies for all calibration stds. (n = 8) ranged from 97-105% (≤5% bias) in human plasma, and the mean inter-day precision for all calibration stds. was less than 8.5%. The mean intra- and inter-day assay accuracy for all quality control (QC) replicates in human plasma (n = 9), determined at each QC level throughout the validated runs, ranged from 96-112% (≤12% bias) and from 102-105% (≤5% bias), resp. The mean intra- and inter-day assay precision was less than 15.0 and 11.8% for all QC levels, resp. For the QC samples prepared in animal species plasma, the %CV values of the assays ranged from 1.8-8.8% in mouse plasma, from 3.7-13.8% in rat plasma, and from 3.0-7.2% in dog plasma. The assay accuracies ranged from 92-102% (≤8% bias) for all QC levels prepared in mouse plasma; ranged from 93-106% (≤7% bias) in rat plasma; and ranged from 95-114% (≤14% bias) in dog plasma. The assay was used to support preclin. pharmacokinetic and toxicokinetic studies and is currently used to measure PM00104 plasma concns. to support clin. trials.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:817412 HCAPLUS Full-text
DOCUMENT NUMBER: 141:307511
TITLE: Antitumor spisulosine compounds
INVENTOR(S): Rinehart, Kenneth L.; Warwick, Robert A.; Avila, Jesus; Fregeau Gallagher, Nancy L.; Garcia Gravalos,

Dolores; Faircloth, Glynn T.
PATENT ASSIGNEE(S): Board of Trustees of the University of Illinois, USA
SOURCE: U.S., 23 pp., Cont.-in-part of U.S. 6,107,520.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6800661	B1	20041005	US 1999-386724		19990831
US 6107520	A	20000822	US 1998-58456		19980410
US 38793	E1	20050906	US 2002-219050		20020814
US 2004147615	A1	20040729	US 2003-693174		20031023
US 2006183806	A9	20060817			
US 7109244	B2	20060919			
US 2006235082	A1	20061019	US 2006-454406		20060615
PRIORITY APPLN. INFO.:			US 1997-43326P	P	19970415
			US 1997-43599P	P	19970415
			US 1998-58456	A2	19980410
			US 1999-386724	A1	19990831
			US 2003-693174	A3	20031023

AB Investigation of the activity of exts. of the clam Spisula polynyma has led to antitumor long-chain, straight-chain alkane or alkene compds. which have a 2-amino group and a 3-hydroxy group. Isolation and preparation of spisulosine compds. are described.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:780551 HCAPLUS Full-text
DOCUMENT NUMBER: 141:254554
TITLE: Aplidine for multiple myeloma treatment
INVENTOR(S): Bertino, Joseph R.; Medina, Daniel; Faircloth, Glynn Thomas; Mitsiades, Constantine S.
PATENT ASSIGNEE(S): Dana-Faber Cancer Institute, Inc., USA; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080477	A1	20040923	WO 2004-GB1062	20040312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004218883	A1	20040923	AU 2004-218883	20040312

CA 2519789	A1	20040923	CA 2004-2519789	20040312
EP 1603584	A1	20051214	EP 2004-720081	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CN 1761480	A	20060419	CN 2004-80006724	20040312
JP 2006519828	T	20060831	JP 2006-505957	20040312
IN 2005DN03454	A	20070817	IN 2005-DN3454	20050803
MX 2005PA09742	A	20060525	MX 2005-PA9742	20050912
NO 2005004668	A	20051011	NO 2005-4668	20051011
US 2006172926	A1	20060803	US 2006-548710	20060411
US 2007149445	A9	20070628		
PRIORITY APPLN. INFO.:			US 2003-454125P P	20030312
			US 2003-520293P P	20031114
			WO 2004-GB1062 W	20040312

AB Aplidine and aplidine analogs are used in the manufacture of a medicament for treating multiple myeloma.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:780508 HCAPLUS Full-text
DOCUMENT NUMBER: 141:271548
TITLE: Improved antitumor treatments using aplidine and aplidine analogs in combination with other drugs
INVENTOR(S): Barnejee, Debabrata; Bertino, Joseph R.; Faircloth, Glynn Thomas; Guray, Saydam; Jimeno, Jose
PATENT ASSIGNEE(S): Pharma Mar S.A., Spain
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080421	A2	20040923	WO 2004-US7606	20040312
WO 2004080421	A3	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004220451	A1	20040923	AU 2004-220451	20040312
CA 2516572	A1	20040923	CA 2004-2516572	20040312
EP 1620117	A2	20060201	EP 2004-720399	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1753684	A	20060329	CN 2004-80005179	20040312
JP 2006519848	T	20060831	JP 2006-507125	20040312
NO 2005003947	A	20051207	NO 2005-3947	20050824
US 2006178298	A1	20060810	US 2005-546750	20051104
PRIORITY APPLN. INFO.:			US 2003-454125P P	20030312

WO 2004-US7606 W 20040312

AB Aplidine and aplidine analogs are of use for the treatment of cancer, in particular in the treatment of leukemias and lymphomas, especially in combination therapies.

L7 ANSWER 11 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:354967 HCAPLUS Full-text
DOCUMENT NUMBER: 140:357671
TITLE: Preparation of kahalalide antitumoral compounds
INVENTOR(S): Faircloth, Glynn Thomas; Elices, Mariano; Sasak, Halina; Aviles Marin, Pablo Manuel; Cuevas Marchante, Maria Del Carmen
PATENT ASSIGNEE(S): Pharma Mar, S.A.U., Spain
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035613	A2	20040429	WO 2003-US33207	20031020
WO 2004035613	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003033012	A1	20030424	WO 2002-GB4735	20021018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2501089	A1	20040429	CA 2003-2501089	20031020
AU 2003285911	A1	20040504	AU 2003-285911	20031020
BR 2003015489	A	20050823	BR 2003-15489	20031020
EP 1572726	A2	20050914	EP 2003-779140	20031020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006517195	T	20060720	JP 2005-501483	20031020
MX 2005PA04133	A	20051005	MX 2005-PA4133	20050418
NO 2005002379	A	20050715	NO 2005-2379	20050513
US 2006234920	A1	20061019	US 2006-531533	20060425

PRIORITY APPLN. INFO.:		
WO 2002-GB4735	A	20021018
GB 2003-4367	A	20030226
GB 2003-14725	A	20030624
US 2001-348449P	P	20011019

WO 2001-GB4821	A	20011031
GB 2002-22409	A	20020926
WO 2003-US33207	W	20031020

AB The invention is directed to new kahalalide antitumoral compds., in particular to analogs of kahalalide F, which are useful as antitumoral, antiviral and antifungal agents and in the treatment of psoriasis. Thus, kahalalide F analogs in which the 5-methylhexanoc acid residue has been replaced by (S)- and (R)-4-methylhexanoic acid were prepared and assayed for cytotoxic activity against various cell lines.

L7 ANSWER 12 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:869631 HCAPLUS Full-text
DOCUMENT NUMBER: 140:210099
TITLE: Use of CFU-GM assay for prediction of human maximum tolerated dose of a new antitumoral drug: Yondelis (ET-743)
AUTHOR(S): Gomez, Susana G.; Bueren, Juan A.; Faircloth, Glynn; Albella, Beatriz
CORPORATE SOURCE: S.A. Poligono Industrial La Mina, PharmaMar, Madrid, 28770, Spain
SOURCE: Toxicology in Vitro (2003), 17(5/6), 671-674
CODEN: TIVIEQ; ISSN: 0887-2333
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Acute cytotoxic exposure causes decreases in bone marrow progenitors that precedes the neutrophil nadir. Expts. in animal models reveal a relationship between the reduction in granulocyte-macrophage progenitors (CFU-GM) and the decrease in absolute neutrophil count [Toxicol. Pathol. 21 (1993) 241]. Recently, the prevalidation of a model for predicting acute neutropenia by the CFU-GM assay has been reported [Toxicol. In Vitro 15 (2001) 729]. The model was based on prediction of human MTD by adjusting the animal-derived MTD for the differential sensitivity between CFU-GM from animal species and humans. In this study, this model has been applied on a new antitumoral drug, Yondelis (Ecteinascidin; ET-743). Preclin. studies showed that hematotoxicity was the main side effect in mice, being the MTD of 600 μg/m2 [Drugs Future 21 (1996) 1155]. The sensitivity of myeloid progenitors was higher in mice than in humans, with IC90 values of 0.69±0.22 nM and 1.31±0.21 nM for murine and human CFU-GMs resp. This study predicts a human MTD of 1145 μg/m2. The reported human MTD of ET-743 given as a 24-h continuous infusion every 3 wk is 1800 μg/m2 [J. Clin. Oncol. 19 (2001) 1256]. Since our predicted MTD is within fourfold of the actual MTD (the interspecies variation in tolerated dose due to differences in clearance rates, metabolism pathways and infusion rate) the result confirms the profit of the prediction model.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:848751 HCAPLUS Full-text
DOCUMENT NUMBER: 140:385585
TITLE: In vitro toxicity of three new antitumoral drugs (trabectedin, aplidin, and kahalalide F) on hematopoietic progenitors and stem cells
AUTHOR(S): Gomez, Susana G.; Bueren, Juan A.; Faircloth, Glynn T.; Jimeno, Jose; Albella, Beatriz
CORPORATE SOURCE: PharmaMar, Madrid, Spain
SOURCE: Experimental Hematology (New York, NY, United States) (2003), 31(11), 1104-1111

CODEN: EXHMA6; ISSN: 0301-472X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: In addition to neutropenias and/or thrombocytopenias as a short-term effect, antineoplastics also can produce long-term effects as a consequence of damage to the hematopoietic stem cells. The aim of the present study was to evaluate the toxicity of three marine-derived antineoplastics on murine hematopoietic stem cells. These antitumoral compds. currently are being evaluated in patients in phase II (aplidin and kahalalide F) and phase II/III (trabectedin) clin. trials. Materials and methods: Long-term competitive repopulating assays were performed in mice to analyze toxic effects on the hematopoietic stem cells responsible for the multipotential long-term repopulation of hematopoiesis. Furthermore, granulocytic and T- and B-lymphoid lineages were studied, as well as myeloid (CFU-GM) and megakaryocytic (CFU-Meg) progenitors. Results: When cells were treated in vitro for 24 h with CFU-GM IC50 dose of trabectedin (9.59 ± 4.96 nM), no significant effects were observed in the stem cells. The dose of trabectedin that produced 90% of inhibition in CFU-GM (IC90: 23.71 ± 1.27 nM) only inhibited 45% survival of stem cells. Doses of aplidin that produced redns. of 50% (56.9 ± 13.32 nM) or 90% (195.88 ± 21.39 nM) in myeloid progenitors did not show any effect on hematopoietic stem cells. Kahalalide F did not show any toxic effect in either short-term or long-term repopulating cells up to 10 μM. Conclusions. Our data show that the hematopoietic stem cells effects of antitumoral drugs can be properly characterized by the murine competitive repopulating assays. Our results suggest that long-term myelosuppression as a consequence of trabectedin, aplidin, or kahalalide F treatment would not be expected.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:638934 HCAPLUS Full-text
DOCUMENT NUMBER: 140:283822

TITLE: Development of a liquid chromatography/tandem mass spectrometry assay for the quantification of Aplidin, a novel marine-derived antineoplastic agent, in human plasma

AUTHOR(S): Yin, Jianming; Aviles, Pablo; Lee, William; Ly, Carl; Floriano, Pablo; Ignacio, Manzanares; Faircloth, Glynn
CORPORATE SOURCE: PharmaMar USA, Inc., Cambridge, MA, 02139-4616, USA

SOURCE: Rapid Communications in Mass Spectrometry (2003), 17(16), 1909-1914
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid and sensitive liquid chromatog./tandem mass spectrometry (LC/MS/MS) assay was developed and validated to quantify a novel marine-derived depsipeptide, Aplidin, in human plasma. The method was validated to demonstrate the specificity, recovery, limit of quantitation (LOQ), accuracy, and precision of measurements. The calibration range for Aplidin was established using Aplidin stds. from 0.05-50 ng/mL in blank human plasma. The multiple reaction monitoring, based on the transition m/z 1110.7→295.3, was specific for Aplidin, and that based on the transition m/z 1112.6→297.3 was specific for didemnin B (the internal standard); no endogenous materials interfered with the anal. of Aplidin and didemnin B from blank human plasma. The assay was linear over the concentration range 0.05-50.0 ng/mL. The

correlation coeffs. for the calibration curves ranged from 0.9979 to 0.9999. The mean intra- and interday accuracies for all calibration stds. (n = 12) ranged from 97 to 106% (≤6% bias), and the mean interday precision for all calibration stds. was less than 8.3%. The mean intra- and interday assay accuracy for all quality control replicates (n = 12), determined at each QC level throughout the validated runs, remained below 12 and 7%, resp. The mean intra- and interday assay precision was less than 13.1 and 10.7% for all QC levels, resp. The assay is currently used to measure Aplidin plasma concns. to support clin. trials.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:584509 HCAPLUS Full-text
DOCUMENT NUMBER: 139:332249
TITLE: Validation of a sensitive assay for thiocoraline in mouse plasma using liquid chromatography-tandem mass spectrometry
AUTHOR(S): Yin, Jianming; Aviles, Pablo; Lee, William; Ly, Carl; Guillen, Maria Jose; Calvo, Pilar; Manzanares, Ignacio; Faircloth, Glynn
CORPORATE SOURCE: PharmaMar USA, Inc., Cambridge, MA, 02139-4616, USA
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 794(1), 89-98
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A sensitive HPLC-tandem mass spectrometry assay for thiocoraline, an antitumor depsipeptide, in mouse plasma is described. Echinomycin, a quinoxaline peptide, was used as an internal standard Thiocoraline was recovered from the mouse plasma using protein precipitation with MeCN and followed by solid-phase extraction of the supernatant. The mobile phase consisted of MeOH (0.1% formic acid)-H2O (0.1% formic acid) (90:10, volume/volume). The anal. column was a YMC C18. The standard curve was linear from 0.1 to 50 ng/mL (R2>0.99). The lower limit of quantitation was 0.1 ng/mL. The assay was specific based on the multiple reaction monitoring transitions at m/z 1157 → 215 and m/z 1101 → 243 for thiocoraline and the internal standard, echinomycin, resp. The mean intra- and inter-day assay accuracies remained <5 and 12%, resp., for all calibration stds. and quality control (QC) samples. The intra- and inter-day assay precisions were <11.4 and 9.5% for all QC levels, resp. The utility of the assay was demonstrated by a pharmacokinetic study of i.v. (bolus) thiocoraline on CD-1 mice. Thiocoraline was stable in mouse plasma in an ice-water bath for 6 h and for three freeze-thaw cycles. The reconstituted thiocoraline after extraction and drying sample process was stable in the autosampler for over 24 h. The assay was able to quantify thiocoraline in plasma up to 48 h following dose. Pharmacokinetic anal. showed that thiocoraline has distinct pharmacokinetic profiling when dosed in different formulation solns. The assay is currently used to measure thiocoraline plasma concns. in support of a project to develop a suitable formulation with a desirable pharmacokinetic profile.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:548630 HCAPLUS Full-text
DOCUMENT NUMBER: 140:174525
TITLE: Effective combination of ET-743 and doxorubicin in

sarcoma: preclinical studies
AUTHOR(S): Meco, Daniela; Colombo, Tina; Ubezio, Paolo; Zucchetti, Massimo; Zaffaroni, Marco; Riccardi, Anna; Faircloth, Glynn; Jose, Jimeno; D'Incalci, Maurizio; Riccardi, Riccardo
CORPORATE SOURCE: Division of Pediatric Oncology, Catholic University of Rome, Rome, Italy
SOURCE: Cancer Chemotherapy and Pharmacology (2003), 52(2), 131-138
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to investigate the cytotoxic and antitumor effects of the combination of the novel anticancer drug ET-743 and doxorubicin (Dx) and to determine whether any pharmacokinetic interaction occurs in sarcoma-bearing mice. The cytotoxicity of each drug and of their combinations was assessed in the rhabdomyosarcoma cell line TE-671 by a clonogenic assay, and isobologram anal. was performed to detect any synergistic, additive or antagonistic effects. The antitumor activities of each drug and of the combinations were also evaluated in nude mice transplanted s.c. with human TE-671 rhabdomyosarcoma and in C3H female mice injected i.v. with UV2237 M fibrosarcoma or with the Dx-resistant subline UV2237 M-ADM which over-expresses Pgp. Antitumor activity was evaluated by monitoring the TE-671 tumor volume over time and, in the case of the murine fibrosarcomas, by evaluation of lung deposits at autopsy quantified by determining lung weight Pharmacokinetic studies were performed in TE-671-bearing mice. ET-743 was determined in plasma by an HPLC-MS method and Dx in plasma and tissue by an HPLC method with fluorescence detection. The combination of ET-743 and Dx was found to be additive with the average combination index slightly lower than 1 at all survival levels, suggesting weak synergism. In TE-671 tumors in vivo the activity of ET-743 or Dx given alone was marginal, whereas the combination produced a significant antitumor effect. The log cell kill (LCK) values were 0.13 and 0.33 for ET-743 and Dx alone, whereas they ranged from 0.85 to 1.12 for the combination. Giving ET-743 1 h before Dx slightly enhanced the effect (LCK 1.12) compared with giving the drugs simultaneously (LCK 0.85) or in the opposite sequence (LCK 0.92). In UV2237 M fibrosarcoma, both Dx and ET-743 showed an effect in reducing the weight of lung metastases, although the combination of the two drugs was not superior to each drug alone. In UV2237 M-ADM tumors neither of the two drugs was active, whereas the combination, particularly when the two drugs were given simultaneously, produced a significant effect. Plasma levels of ET-743 and Dx were not significantly different when the drugs were given alone or in combination. The concns. of Dx in tissues including tumor, liver, heart and kidney were found to be the same whether the drug was given alone or in combination with ET-743. These results indicate that ET-743 and Dx in combination produce an additive effect against human sarcoma cells, reinforcing the idea that they act by a different mechanism of action. In mice no pharmacokinetic interaction between the two drugs was found. The observed activity in UV2237 M-ADM and in human TE-671 sarcoma suggests that the combination of the two drugs could be effective for tumors displaying low sensitivity to each drug given alone. Based on these findings a phase I study on the combination of the two drugs was recently initiated.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:196182 HCAPLUS Full-text
DOCUMENT NUMBER: 139:285666
TITLE: Antiangiogenesis Treatment Combined with Chemotherapy

Produces Chondrosarcoma Necrosis
AUTHOR(S): Morioka, Hideo; Weissbach, Lawrence; Vogel, Tikva; Nielsen, G. Petur; Faircloth, Glynn T.; Shao, Li; Hornicek, Francis J.
CORPORATE SOURCE: Orthopedic Research Laboratories, Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Clinical Cancer Research (2003), 9(3), 1211-1217
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A combination therapy protocol using a marine chemotherapeutic and antiangiogenic mol. was tested in a mouse tumor xenograft model for the ability to curtail the growth of a human chondrosarcoma (CHSA). Ecteinascidin-743 (ET-743), a marine-derived chemotherapeutic, was effective at slowing the growth of a primary CHSA. Plasminogen-related protein B, which antagonizes various endothelial cell activities, also elicited a significant inhibition of neoplastic growth, albeit with reduced effectiveness. The combination of the two agents resulted in only a modest further repression of tumor growth over that associated with ET-743 treatment alone, as measured by tumor volume (82% vs. 76% inhibition, resp.). However, anal. of the extent of tumor necrosis and vascularization of the tumor revealed that the coadministration of the two compds. was clearly more effective, eliciting a 2.5-fold increase in tumor necrosis relative to single-agent treatment. The combination therapy also was most effective at antagonizing tumor-associated microvessel formation, as assessed by CD31 immunostaining, suggesting that combination therapy may hold promise for treating CHSA. Tumor necrosis produced by combination therapy of ET-743 and recombinant plasminogen-related protein B was also significantly greater than that produced by conventional doxorubicin treatment, further corroborating the efficacy of combination therapy.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:974072 HCAPLUS Full-text
DOCUMENT NUMBER: 139:127523
TITLE: Effectiveness of ecteinascidin-743 against drug-sensitive and -resistant bone tumor cells
AUTHOR(S): Scotlandi, Katia; Perdichizzi, Stefania; Manara, Maria Cristina; Serra, Massimo; Benini, Stefania; Cerisano, Vanessa; Strammiello, Rosaria; Mercuri, Mario; Reverter-Branchat, Gemma; Faircloth, Glynn; D'Incalci, Maurizio; Picci, Piero
CORPORATE SOURCE: Laboratorio di Ricerca Oncologica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Clinical Cancer Research (2002), 8(12), 3893-3903
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The identification of new drugs is strongly needed for bone tumors. Ecteinascidin-743 (ET-743), a highly promising antitumor agent isolated from the marine tunicate Ecteinascidia turbinata, is currently under Phase II clin. investigation in Europe and the United States for treatment of soft tissue sarcoma. In this study, we analyzed the preclin. effectiveness of this drug in osteosarcoma and Ewing's sarcoma. The effects of ET-743 were evaluated against a panel of human osteosarcoma and Ewing's sarcoma cell lines characterized by different drug responsiveness and compared with the effects of standard anticancer agents. In addition, combination treatments with ET-743 and the other standard chemotherapy agents for sarcoma were analyzed to

highlight the best drug-to-drug interaction. A potent activity of ET-743 was clearly observed against both drug-sensitive and drug-resistant (multidrug-resistant, methotrexate- and cisplatin-resistant) bone tumor cells at concns. that are easily achievable in patients (pM to nM range). Ewing's sarcoma cells appeared to be particularly sensitive to the effects of this drug. The anal. of the effects of ET-743 on cell cycle, apoptosis, and differentiation indicated that both osteosarcoma and Ewing's sarcoma cells had a slower progression through the different phases of the cell cycle after treatment with ET-743. However, the drug was able to induce a massive apoptosis in Ewing's sarcoma but not in osteosarcoma cells. In the latter neoplasm, ET-743 showed a differential effect, as indicated by the significant increase in the expression and activity of alkaline phosphatase, a marker of osteoblastic differentiation. Concurrent exposure of cells to ET-743 and other chemotherapeutic agents resulted in greater than additive interactions when doxorubicin and cisplatin were used, whereas subadditive effects were observed with methotrexate, vincristine, and actinomycin D. Overall, these results encourage the inclusion of this drug in the treatment of patients with bone tumors, although a careful design of new regimens is required to identify the best therapeutic conditions.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:742571 HCAPLUS Full-text
DOCUMENT NUMBER: 139:62716
TITLE: Preclinical toxicity studies of kahalalide F, a new anticancer agent: single and multiple dosing regimens in the rat
AUTHOR(S): Brown, Alan P.; Morrissey, Robert L.; Faircloth, Glynn T.; Levine, Barry S.
CORPORATE SOURCE: Toxicology Research Laboratory, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2002), 50(4), 333-340
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kahalalide F (KF) is a new anticancer agent currently in clin. trials for solid tumors, including prostate cancer. During the preclin. development of this drug, the studies reported here were conducted to determine the acute and multiple dose toxicities of KF when administered i.v. to rats. This dosing route is the intended route of clin. administration. KF was administered i.v. to male and female CD rats using single- and multiple-dose (daily for 5 days) schedules. Animals were observed for clin. signs, and body weight, hematol., and clin. chemical parameters determined Animals were necropsied, gross observations and organ wts. recorded, and numerous tissues were collected and examined microscopically. KF produced lethality at 375 and 450 μg/kg in males and females, resp., and the maximum tolerated dose (MTD) was estimated to be 300 μg/kg (1800 μg/m2). The nervous system appeared to be a potential site of action for the production of lethality. Single-dose administration of KF at 150 and 300 μg/kg produced organ toxicity in which the kidney was the primary target. Injury to distal convoluted tubules was the most toxicol. significant lesion, and was observed on day 4. However, by day 29, resolution of renal toxicity had occurred in the 150-μg/kg group, but only partial resolution was seen at 300 μg/kg. Renal injury correlated with increased serum creatinine, BUN, and kidney wts. at 300 μg/kg, indicating impairment of renal function. Subacute, necrotizing inflammation of bone marrow and peritrabecular osteocyte hyperplasia of bone were seen at 300 μg/kg on day 4, with recovery thereafter.

Injury to blood vessels and surrounding tissue at the injection site were produced by KF, likely due to local cytotoxicity. In general, reversibility of toxicity was seen at 150 μg/kg but not at 300 μg/kg. When KF was administered once daily for five consecutive days at a dose of 80 μg/kg per day (400 μg/kg total dose), slightly decreased body weight gain was the primary drug-related effect. Therefore, the no-adverse-effect dose was at or near 80 μg/kg per day (480 μg/m2 per day). These findings demonstrate that fractionation of a lethal or MTD dose of KF by daily administration for 5 days reduces drug-induced toxicity, and appears to be a viable option for the clin. evaluation of KF for the treatment of cancer.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:526235 HCAPLUS Full-text
DOCUMENT NUMBER: 138:100185
TITLE: Unique features of the mode of action of ET-743
AUTHOR(S): D'Incalci, Maurizio; Erba, Eugenio; Damia, Giovanna; Galliera, Emanuela; Carrassa, Laura; Marchini, Sergio; Mantovani, Roberto; Tognon, Gianluca; Fruscio, Robert; Jimeno, Jose; Faircloth, Glynn T.
CORPORATE SOURCE: Department of Oncology, Istituto di Ricerche Farmacologiche "Mario Negri,", Milan, 20157, Italy
SOURCE: Oncologist (2002), 7(3), 210-216
CODEN: OCOLF6; ISSN: 1083-7159
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review of the current knowledge of the primary mode of action of a natural product, ecteinascidin 743 (ET-743), derived from the marine tunicate Ecteinascidia turbinata. ET-743 was initially selected for preclin. development because of its potent antitumor activity observed against several human solid tumor types. In vitro, the drug is cytotoxic in the nanomolar range, and in the case of some very sensitive cell lines, in the picomolar range. The large potency differences observed among several solid tumor types indicate that this compound possesses some tumor selectivity, but the mol. basis of these differential effects remains to be elucidated. The the mechanism of action of ET-743 is evaluated in this context. The available information on ET-743 binding to DNA and its effects on transcriptional regulation point to a unique behavior of this drug, as it independently affects specific gene transcription in a promoter-dependent way. In addition, ET-743 shows a peculiar pattern of selectivity in cells with different defects in their DNA-repair pathways. These results highlight a unique property of ET-743, possibly explaining why it possesses antitumor activity against tumors that are refractory to standard anticancer drugs, all of which certainly act by mechanisms that are different from that of ET-743.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:353299 HCAPLUS Full-text
DOCUMENT NUMBER: 136:359641
TITLE: Kahalalide F formulations for antitumor use
INVENTOR(S): Ruffles, Graham Keith; Faircloth, Glynn Thomas ; Nuyen, Bastian; Weitman, Steve
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002036145	A2	20020510	WO 2001-GB4821		20011031
WO 2002036145	A3	20021017			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2425627	A1	20020510	CA 2001-2425627		20011031
AU 200210749	A	20020515	AU 2002-10749		20011031
EP 1330258	A2	20030730	EP 2001-978654		20011031
EP 1330258	B1	20051228			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001014912	A	20031014	BR 2001-14912		20011031
JP 2004512370	T	20040422	JP 2002-538956		20011031
CN 1568192	A	20050119	CN 2001-818271		20011031
NZ 525243	A	20050128	NZ 2001-525243		20011031
AT 314084	T	20060115	AT 2001-978654		20011031
HU 200600031	A2	20060529	HU 2006-31		20011031
ES 2256305	T3	20060716	ES 2001-1978654		20011031
RU 2292216	C2	20070127	RU 2003-116124		20011031
CA 2462639	A1	20030424	CA 2002-2462639		20021018
WO 2003033012	A1	20030424	WO 2002-GB4735		20021018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002334203	A1	20030428	AU 2002-334203		20021018
EP 1435990	A1	20040714	EP 2002-801430		20021018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
ZA 2003003136	A	20040723	ZA 2003-3136		20030423
NO 2003001860	A	20030630	NO 2003-1860		20030425
MX 2003PA03704	A	20040504	MX 2003-PA3704		20030425
HK 1054192	A1	20060908	HK 2003-106441		20030910
US 2004067895	A1	20040408	US 2003-399571		20031114
PRIORITY APPLN. INFO.:			US 2000-244471P	P	20001031
			US 2000-246229P	P	20001106
			US 2001-348449P	P	20011019
			WO 2001-GB4821	W	20011031
			GB 2002-22409	A	20020926
			WO 2002-GB4735	W	20021018

AB New formulations and new uses of kahalalide F are provided for antitumor application against neuroblastomas or dedifferentiated or mesenchymal chondrosarcomas or osteosarcomas.

L7 ANSWER 22 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:817226 HCAPLUS Full-text
DOCUMENT NUMBER: 135:362533
TITLE: Immunosuppressive sesbanimide compositions
INVENTOR(S): Faircloth, Glynn T.; Millan, Francisco Romero; Fernandez, Librada Maria Canedo; Sarabia, Cristina Accbal
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont. of U.S. Ser. No. 53,485, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001039041	A1	20011108	US 2001-756244	20010108
PRIORITY APPLN. INFO.:			US 1995-479695 B1	19950607
			US 1998-53485 B1	19980401

AB The active component of the pharmaceutical composition of the present invention is a compound which has been isolated from the controlled aerobic fermentation of a marine microorganism, Agrobacterium sp. The pharmaceutical compns. of the present invention, useful for postsurgical graft tolerance, are thus directed to compns. comprising a pharmaceutical carrier, diluent or excipient, and an effective amount of sesbanimide, which is an alkaloid that has been previously been isolated from seeds and reported to be useful as an antitumor drug. Prior to the present invention however, this compound had not been isolated from any fermentation broth nor had it been determined to have immunomodulatory activity. The crude residue of fermented Agrobacterium species was dissolved in H2O-MeOH (1:1). The water/alc. fraction was extracted twice with CH2Cl2 and twice with EtOAc. The organic solvent-soluble components were concentrated yielding active organic exts. The organic extract was chromatographed on silica gel by an MPLC system using a mixture of hexane/EtOAc as the eluting solvent. The immunosuppressive and antitumor activities were detected in some of the fractions.

L7 ANSWER 23 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:750175 HCAPLUS Full-text
DOCUMENT NUMBER: 136:395455
TITLE: Sensitivity of soft tissue sarcoma cell lines to chemotherapeutic agents: identification of ecteinascidin-743 as a potent cytotoxic agent
AUTHOR(S): Li, Wei Wei; Takahashi, Naoto; Jhanwar, Suresh; Cordon-Cardo, Carlos; Elisseyeff, Yaroslav; Jimeno, Jose; Faircloth, Glynn; Bertino, Joseph R.
CORPORATE SOURCE: Laboratories of Molecular Pharmacology, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Clinical Cancer Research (2001), 7(9), 2908-2911
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cytotoxic effects of ecteinascidin-743(ET-743), a novel marine natural product, were evaluated and compared with that of clin. used anticancer agents methotrexate, doxorubicin, etoposide, and paclitaxel in eight human soft tissue sarcoma (STS) cell lines. HT-1080, a fibrosarcoma cell line, and HS-42, a malignant mesodermal cell line, were the most sensitive of the cell lines to methotrexate, doxorubicin, etoposide, and paclitaxel. Other cell lines (IC50s) varied considerably and were more resistant to these agents. ET-743 was more potent than any of these agents, with IC50s in the PM range in all of the cell lines. Cytotoxicity of ET-743 was dose- and time-related (4-72 h exposure). Cytotoxic concns. of ET-743 produced a S/G2 block in all of the cell lines tested. Three colon adenocarcinoma cell lines, HCT-8, HT-29, and HCT-116, and one breast cancer cell line, MCF-7, were 1-2 logs less sensitive to ET-743 than the STS cell lines. Cell lines were also characterized as to expression of oncogenes and tumor suppressor genes to attempt to correlate sensitivity of these cell lines to ET-743 and other chemotherapeutic agents. All of the cell lines except M8805, a malignant fibrous histiocytoma cell line, had mutations in p53 and/or overexpressed the MDM2 protein. Only HS-18, a liposarcoma cell line, lacked expression of the retinoblastoma protein. None of the cell lines had detectable expression of P-glycoprotein as measured by immunohistochem. ET-743 is an extremely potent cytotoxic agent against human STS cell lines and is being evaluated as an antitumor agent in this disease.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:380410 HCAPLUS Full-text

DOCUMENT NUMBER: 134:361352

TITLE: Aplidine for treatment of cancers

INVENTOR(S): Faircloth, Glynn Thomas; Twelves, Chris; Paz-Ares, Luis

PATENT ASSIGNEE(S): Pharma Mar S.A., Spain

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035974	A2	20010525	WO 2000-GB4349	20001115
WO 2001035974	A3	20011101		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2391502	A1	20010525	CA 2000-2391502	20001115
BR 2000015811	A	20020806	BR 2000-15811	20001115
EP 1229922	A2	20020814	EP 2000-976137	20001115
EP 1229922	B1	20070606		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200203906	A2	20030328	HU 2002-3906	20001115

JP 2003514025	T	20030415	JP 2001-537965	20001115
NZ 518847	A	20040227	NZ 2000-518847	20001115
AU 780417	B2	20050317	AU 2001-14023	20001115
RU 2261104	C2	20050927	RU 2002-115864	20001115
AT 363910	T	20070615	AT 2000-976137	20001115
CA 2424823	A1	20020418	CA 2001-2424823	20011012
WO 2002030441	A2	20020418	WO 2001-GB4555	20011012
WO 2002030441	A3	20020801		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 200194024	A	20020422	AU 2001-94024	20011012
EP 1330254	A2	20030730	EP 2001-974510	20011012
EP 1330254	B1	20050706		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001014604	A	20031014	BR 2001-14604	20011012
HU 200302293	A2	20031128	HU 2003-2293	20011012
JP 2004510824	T	20040408	JP 2002-533881	20011012
NZ 525196	A	20040924	NZ 2001-525196	20011012
AT 299028	T	20050715	AT 2001-974510	20011012
ES 2243555	T3	20051201	ES 2001-1974510	20011012
AU 2001294024	B2	20060105	AU 2001-294024	20011012
NO 2002002293	A	20020705	NO 2002-2293	20020514
MX 2002PA04862	A	20030128	MX 2002-PA4862	20020515
BG 106714	A	20030228	BG 2002-106714	20020518
NO 2003001673	A	20030612	NO 2003-1673	20030411
MX 2003PA03230	A	20041203	MX 2003-PA3230	20030411
US 2004010043	A1	20040115	US 2003-398835	20030801

PRIORITY APPLN. INFO.:	GB 1999-27006	A	19991115
	GB 2000-5701	A	20000309
	GB 2000-7639	A	20000329
	GB 2000-15496	A	20000623
	GB 2000-25209	A	20001013
	GB 2000-25044	A	20001012
	WO 2000-GB4349	W	20001115
	GB 2001-7373	A	20010323
	WO 2001-GB4555	W	20011012

AB Aplidine demonstrates considerable promise in phase I clin. trials for treatment of tumors, and various dosing regimes are given. Tumor reduction has been observed in several tumor types including renal carcinoma, colorectal cancer, lung carcinoid, medullary thyroid carcinomas and melanoma. It has also been found that aplidine has a role in inhibiting angiogenesis, complementing the antitumor activity.

L7 ANSWER 25 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:363160 HCAPLUS Full-text
DOCUMENT NUMBER:	136:130300
TITLE:	Unique pattern of ET-743 activity in different cellular systems with defined deficiencies in DNA-repair pathways
AUTHOR(S):	Damia, Giovanna; Silvestri, Simonetta; Carrassa, Laura; Filiberti, Laura; Faircloth, Glynn T.

; Liberi, Giordano; Foiani, Marco; D'Incalci, Maurizio
CORPORATE SOURCE: Department of Oncology, Instituto di Ricerche Farmacologiche "Mario Negri", Milan, 20157, Italy
SOURCE: International Journal of Cancer (2001), 92(4), 583-588
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cytotoxic activity of ecteinascidin 743 (ET-743), a natural product derived from the marine tunicate Ecteinascidia turbinata that exhibits potent anti-tumor activity in pre-clin. systems and promising activity in phase I and II clin. trials, was investigated in a number of cell systems with well-defined deficiencies in DNA-repair mechanisms. ET-743 binds to N2 of guanine in the minor groove, but its activity does not appear to be related to DNA-topoisomerase I poisoning as the drug is equally active in wild-type yeast and in yeast with a deletion in the DNA-topoisomerase I gene. Defects in the mismatch repair pathway, usually associated with increased resistance to methylating agents and cisplatin, did not affect the cytotoxic activity of ET-743. However, ET-743 did show decreased activity (from 2- to 8-fold) in nucleotide excision repair (NER)-deficient cell lines compared to NER-proficient cell lines, from either hamsters or humans. Restoration of NER function sensitized cells to ET-743 treatment. The DNA double-strand-break repair pathway was also investigated using human glioblastoma cell lines MO59K and MO59J, resp., proficient and deficient in DNA-dependent protein kinase (DNA-PK), ET-743 was more effective in cells lacking DNA-PK; moreover, pre-treatment of HCT-116 colon carcinoma cells with wortmannin, a potent inhibitor of DNA-PK, sensitized cells to ET-743. An increase in ET-743 sensitivity was also observed in ataxia telangiectasia-mutated cells. The data strongly suggest that ET-743 has a unique mechanism of interaction with DNA.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:855753 HCAPLUS Full-text
DOCUMENT NUMBER: 134:25353
TITLE: Uses of didemnins as immunomodulating agents
INVENTOR(S): Rinehart, Kenneth L.; Faircloth, Glynn
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 17 pp., Cont. of U.S. Ser. No. 664,234, abadoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6156724	A	20001205	US 1998-111190	19980707
PRIORITY APPLN. INFO.:			US 1996-664234	B1 19960607

AB The invention is based on the immunomodulatory activity of synthetic and semi-synthetic didemnin compds. Certain didemnin compds. possess unexpectedly high immunomodulation activity and will be useful for modulating or regulating immunol. functions in warm-blooded animals. From the data provided, it is believed that the physician will be able to determine the appropriate dosage of the immunosuppressant didemnins of the present invention. The actual dosage to be administered depends, inter alia, on the animal species to be treated, the subject animal's size, and the capacity of the subject to use the particular didemnin compound administered. Accordingly, the actual amts. of

any didemnin compound required to be administered depend on the judgment of the practitioner.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 27 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:412188 HCAPLUS Full-text
DOCUMENT NUMBER: 133:129636
TITLE: Interference of transcriptional activation by the antineoplastic drug ecteinascidin-743
AUTHOR(S): Minuzzo, Mario; Marchini, Sergio; Broggini, Massimo; Faircloth, Glynn; D'Incalci, Maurizio; Mantovani, Roberto
CORPORATE SOURCE: Dipartimento di Genetica e di Biologia dei Microrganismi, Universita degli Studi di Milano, Milan, 20133, Italy
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(12), 6780-6784
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ecteinascidin-743 (ET-743) is a tetrahydroisoquinoline alkaloid isolated from the tunicate Ecteinascidia turbinata currently under phase II clin. trials for its potent anticancer activity. ET-743 binds DNA in the minor groove and forms covalent adducts with some sequence specificity. It selectively inhibits in vitro binding of the CCAAT box factor NF-Y. In this study, the authors assayed ET-743 function in vivo on the HSP70 promoter. On heat induction, the drug blocks transcription rapidly at pharmacol. concns. and in a CCAAT-dependent manner, whereas the activity of the CCAAT-less simian virus 40 promoter is not affected. The effect is exerted at the mRNA level. The distamycin-like alkylating tallimustine is inactive in these assays. Binding of NF-Y and of the heat-shock factor is normal in ET-743-treated cells. Run-on anal. of several endogenous genes further proves that the drug has rapid, profound, and selective neg. effects on transcription. Thus, this marine-derived compound is a promoter-specific, transcription-interfering agent.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 28 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:412185 HCAPLUS Full-text
DOCUMENT NUMBER: 133:129635
TITLE: Ecteinascidin 743, a transcription-targeted chemotherapeutic that inhibits MDR1 activation
AUTHOR(S): Jin, Shengkan; Gorfajn, Barbara; Faircloth, Glynn; Scotto, Kathleen W.
CORPORATE SOURCE: Molecular Pharmacology and Therapeutics Program, Memorial Sloan-Kettering Cancer Center and the Weill Graduate School of Medical Sciences of Cornell University, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(12), 6775-6779
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ecteinascidin 743 (ET-743), a highly promising marine-based anti-tumor agent presently in phase II clin. trials, has been shown to interfere with the binding of minor-groove-interacting transcription factors, particularly NF-Y, with their cognate promoter elements in vitro. The authors have shown that

NF-Y is a central mediator of activation of transcription of the human P glycoprotein gene (MDR1) by a variety of inducers and that NF-Y functions by recruiting the histone acetyltransferase PCAF to the MDR1 promoter. In the present study, the authors tested whether ET-743 could block activation of the MDR1 promoter by agents that mediate their effect through the NF-Y/PCAF complex. The authors report that physiol. relevant concns. of ET-743 abrogate transcriptional activation of both the endogenous MDR1 gene and MDR1 reporter constructs by the histone deacetylase inhibitors as well as by UV light, with minimal effect on constitutive MDR1 transcription. Notably, this inhibition does not alter the promoter-associated histone hyperacetylation induced by histone deacetylase inhibitors, suggesting an in vivo mol. target downstream of NF-Y/PCAF binding. ET-743 is therefore the prototype for a distinct class of transcription-targeted chemotherapeutic agents and may be an efficacious adjuvant to the treatment of multidrug-resistant tumors.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:672566 HCAPLUS Full-text
DOCUMENT NUMBER: 131:295576
TITLE: Spisulosine compounds having antitumor activity
INVENTOR(S): Rinehart, Kenneth Lloyd; Fregeau, Nancy Louise; Warwick, Robert Arthur; Garcia Gravalos, Dolores; Avila, Jesus; Faircloth, Glynn Thomas
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA; Ruffles, Graham Keith
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952521	A1	19991021	WO 1999-GB1091	19990409
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6107520	A	20000822	US 1998-58456	19980410
CA 2328126	A1	19991021	CA 1999-2328126	19990409
AU 9934321	A	19991101	AU 1999-34321	19990409
AU 763981	B2	20030807		
BR 9910120	A	20001226	BR 1999-10120	19990409
TR 200002955	T2	20010122	TR 2000-200002955	19990409
EP 1069894	A1	20010124	EP 1999-915898	19990409
EP 1069894	B1	20050831		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002511410	T	20020416	JP 2000-543131	19990409
HU 200105443	A2	20020729	HU 2001-5443	19990409
NZ 507349	A	20021220	NZ 1999-507349	19990409
RU 2225710	C2	20040320	RU 2000-128037	19990409
AT 303139	T	20050915	AT 1999-915898	19990409
ES 2248995	T3	20060316	ES 1999-915898	19990409

NO 2000005052	A	20001207	NO 2000-5052		20001006
MX 2000PA09930	A	20020424	MX 2000-PA9930		20001010
BG 104935	A	20010731	BG 2000-104935		20001109
BG 64970	B1	20061130			
PRIORITY APPLN. INFO.:			US 1998-58456	A	19980410
			US 1997-43326P	P	19970415
			US 1997-43599P	P	19970415
			WO 1999-GB1091	W	19990409

AB Investigation of the activity of exts. of the clam Spisula polynyma has led to antitumor long-chain, straight-chain alkane or alkene compds. which have a 2-amino group and a 3-hydroxy group.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 30 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:625555 HCAPLUS Full-text
DOCUMENT NUMBER: 131:317437
TITLE: Effect of ecteinascidin-743 on the interaction between DNA binding proteins and DNA
AUTHOR(S): Bonfanti, Marina; La Valle, Elisa; Faro, Jose-Maria Fernandez Sousa; Faircloth, Glynn; Caretti, Giuseppina; Mantovani, Roberto; D'Incalci, Maurizio
CORPORATE SOURCE: Department of Oncology, Istituto di Ricerche Farmacologiche Mario Negri, Milan, 20157, Italy
SOURCE: Anti-Cancer Drug Design (1999), 14(3), 179-186
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ecteinascidin-743 (ET-743) is a tetrahydroisoquinoline alkaloid isolated from Ecteinascidia turbinata, a tunicate growing in mangrove roots in Caribbean. It has been shown to bind in the minor groove of DNA forming covalent adducts by reaction of the N2 of guanine with the carbinolamine moiety. We investigated ET-743 ability to inhibit the binding of different transcription factors to their consensus sequences by using gel shift assays. We have selected three types of factors: (i) oncogene products such as MYC, c-MYB and Maf; (ii) transcriptional activators regulated during the cell cycle as E2F and SRF; and (iii) general transcription factors such as TATA binding protein (TBP), Sp1 and NF-Y. We observed no inhibition of the binding of Sp1, Maf, MYB and MYC. Inhibition of DNA binding was observed for TBP, E2F, SRF at ET-743 concns. ranging from 50 to 300 μM. The inhibition of binding of NF-Y occurs at even lower concns. (i.e. 10-30 μM) when the recombinant subunits of NF-Y are preincubated with the drug, indicating that the inhibition of NF-Y binding does not require previous ET-743 DNA binding. Since NF-Y is a trimer containing two subunits with high resemblance to histones H2B and H2A, we have investigated the effect of ET-743 on nucleosome reconstitution. ET-743 caused a decrease of the nucleosomal band at 100 nM, with the complete disappearance of the band at 3-10 μM. These data suggest that the mode of action of this novel anticancer drug is related to its ability to modify the interaction between some DNA binding proteins and DNA.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:566537 HCAPLUS Full-text
DOCUMENT NUMBER: 131:208780
TITLE: Cytotoxicity and neurocytotoxicity of new marine anticancer agents evaluated using in vitro assays
AUTHOR(S): Geldof, Albert A.; Mastbergen, Simon C.; Henrar,

Roland E. C.; Faircloth, Glynn T.
CORPORATE SOURCE: Dep. Urology/Nuclear Med., Vrije Univ. Amsterdam, Amsterdam, 1007 MB, Neth.
SOURCE: Cancer Chemotherapy and Pharmacology (1999), 44(4), 312-318
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New classes of anticancer drugs, isolated from marine organisms, were shown to possess cytotoxic activity against multiple tumor types. Aplidine, didemnin B, and isohomohalichondrin B (IHB), among the more promising antitumor candidates, were evaluated in the present study on a comparative basis in terms of their antiproliferative activity and neurotoxic effects in vitro. Using a panel of different human prostatic cancer cell lines (DU 145, PC-3, and LNCaP-FGC) the effects of aplidine, didemnin B, and IHB on tumor cell proliferation were tested in a colorimetric (XTT) assay and compared with the effects of vincristine, vinorelbine, and taxol. Under analogous in vitro conditions these drugs were also monitored for neurocytotoxic effects using a PC 12 cell line based model. Didemnin B and - especially aplidine were more effective in the inhibition of prostate cancer cell proliferation than vincristine, vinorelbine, or taxol at concentration levels between 5-50 pmol/mL. At these same concns., however, didemnin B and aplidine were also most potent in the in vitro neurotoxicity assays. IHB was found to exert even more potent antiproliferative activity (at concentration levels between 0.05-0.1 pmol/mL). However, neurotoxic effects were also found to be present at these levels. After drug withdrawal, the neurotoxic damage, inflicted by aplidine or IHB appeared to be more long lasting than after vincristine or vinorelbine exposure. These results point to high antiproliferative activity of aplidine and IHB in prostate cancer. At the same time, the data urge some caution in the clin. use of these agents because of potential neurotoxic side-effects. The use of a newly formulated aplidine may involve a more favorable therapeutic profile.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 32 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:432824 HCAPLUS Full-text
DOCUMENT NUMBER: 131:179198
TITLE: Bioanalysis of aplidine, a new marine antitumoral depsipeptide, in plasma by high-performance liquid chromatography after derivatization with trans-4'-hydrazino-2-stilbazole
AUTHOR(S): Sparidans, Rolf W.; Kettenes-Van Den Bosch, J. Jantien; Van Tellingen, Olaf; Nuyen, Bastiaan; Henrar, Roland E. C.; Jimeno, Jose M.; Faircloth, Glynn; Floriano, Pablo; Rinehart, Kenneth L.; Beijnen, Jos H.
CORPORATE SOURCE: Faculty of Pharmacy, Department of Pharmaceutical Analysis, Utrecht University, Utrecht, 3584 CA, Neth.
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 729(1 + 2), 43-53
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sensitive bio-anal. assay in plasma of the depsipeptide aplidine is reported, based on reversed-phase liquid chromatog. and fluorescence detection of the trans-4'-hydrazino-2-stilbazole (4'H2S) derivative of the analyte. At ambient temperature, two conformations of the depsipeptide are observed in

solution due to cis-trans isomerism at the proline-pyruvoyl peptide bond. Aplidine is isolated from the matrix by solid-phase extraction on an octadecyl modified silica stationary phase. After evaporation of the acetone eluate, a derivatization with 4'H2S is performed in a water-acetonitrile mixture at pH 4. The reaction mixture is injected directly into the chromatograph and the analyte is quantified by fluorescence detection at 410 and 560 nm for excitation and emission, resp. The method has been validated in the 2-100 ng/mL-range, 2 ng/mL being the lower limit of quantification. Precision and accuracy both meet the current requirements for a bioanal. assay. The identity of the 4'H2S reaction products of aplidine have been confirmed by mass spectrometric anal. Finally, the method has been employed for a pilot pharmacokinetic study of aplidine in mice which demonstrated its usefulness for pharmacol. research.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:300619 HCAPLUS Full-text
DOCUMENT NUMBER: 131:82490
TITLE: Bioanalysis of thiocoraline, a new marine antitumoral depsipeptide, in plasma by high-performance liquid chromatography and fluorescence detection
AUTHOR(S): Sparidans, Rolf W.; Henrar, Roland E. C.; Jimeno, Jose M.; Faircloth, Glynn; Floriano, Pablo; Beijnen, Jos H.
CORPORATE SOURCE: Faculty of Pharmacy, Department of Pharmaceutical Analysis, Utrecht University, Utrecht, 3584 CA, Neth.
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 726(1 + 2), 255-260
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sensitive bioanal. assay for thicoraline, an investigational marine anticancer agent, in plasma, based on reversed-phase liquid chromatog. and fluorescence detection, is reported. The proteins in the sample are precipitated by the addition of acetonitrile. After centrifugation, the supernatant is injected directly into the chromatograph. The analyte is quantified by fluorescence detection with excitation and emission at 365 and 540 nm, resp. The method has been validated in the 1-100 ng/mL range, 1 ng/mL being the lower limit of quantification. Precision and accuracy both meet the current requirements for a bio-anal. assay and are <15% at 1 ng/mL and ≤5% in the 5-100 ng/mL range. Plasma samples can be stored for at least 4 mo at -800C. Finally, the usefulness of this method for pharmacol. research was shown in a pilot study of the pharmacokinetics of thiocoraline in rats.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 34 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:744958 HCAPLUS Full-text
DOCUMENT NUMBER: 130:10633
TITLE: Aplidine as an L-type calcium channel enhancer
INVENTOR(S): Crumb, William J.; Faircloth, Glynn T.
PATENT ASSIGNEE(S): Pharma Mar, S.A., Spain
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9850048	A1	19981112	WO 1998-US9238		19980506
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2288639	A1	19981112	CA 1998-2288639		19980506
AU 9872900	A	19981127	AU 1998-72900		19980506
AU 740598	B2	20011108			
US 6030943	A	20000229	US 1998-73288		19980506
EP 981352	A1	20000301	EP 1998-920293		19980506
R: AT, BE, CH, DE, DK, ES, GB, IT, LI, SE, PT, IE, FI					
JP 2001526657	T	20011218	JP 1998-548441		19980506
PRIORITY APPLN. INFO.:			US 1997-45803P	P	19970507
			WO 1998-US9238	W	19980506

AB This invention relates to a cardiotonic effect of Aplidine (dehydrodidemnin B). Aplidine has been found to be a potent L-type calcium channel enhancer in the human heart. This effect makes Aplidine a very useful drug for the treatment of congestive heart failure, as well as useful for the treatment of atrial fibrillation. Extraction and isolation if Aplidine from Aplidium albicans, its semisynthesis from didemnin B, and its synthesis from pyruvyl-Pro-OBz and EDC or DMAP are presented.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:565299 HCAPLUS Full-text
DOCUMENT NUMBER: 129:270190
TITLE: Ecteinascidin-743, a new marine natural product with potent antitumor activity on human ovarian carcinoma xenografts
AUTHOR(S): Valoti, Giorgio; Nicoletti, M. Ines; Pellegrino, Antonio; Jimeno, Jose; Hendriks, Hans; D'Incalci, Maurizio; Faircloth, Glynn; Giavazzi, Raffaella
CORPORATE SOURCE: Mario Negri Institute for Pharmacological Research, Bergamo, Italy
SOURCE: Clinical Cancer Research (1998), 4(8), 1977-1983
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor activity of ecteinascidin (ET)-743, a novel marine natural product, was evaluated against a panel of human ovarian carcinoma xenografts characterized by different malignant behaviors and drug responsiveness in nude mice. These tumor models included three xenografts transplanted s.c. (HOC18, HOC22-S, and MNB-PTX-1) into nude mice, representing different levels of sensitivity to cisplatinum (DDP), which was used as reference drug for ovarian carcinoma, and two other xenografts (HOC22 and HOC8), which are highly malignant in the peritoneal cavity of nude mice, representing the growth pattern of this neoplasm. At the maximum tolerated dose of 0.2 mg/kg using an intermittent schedule of one i.v. injection every 4 days, ET-743 was highly active against HOC22-S (sensitive to DDP), inducing long-lasting, complete regressions, and against HOC18 (marginally sensitive to DDP), inducing partial

tumor regressions. Moreover, significant growth delay was observed in mice bearing late-stage HOC18 tumor (400-mg tumor weight; nonresponsive to DDP). ET-743, however, was not active against MNB-PTX-1, a tumor that is highly resistant to chemotherapy, including DDP. In the i.p. ovarian carcinoma xenograft model, ET-743 at the maximum tolerated dose induced complete tumor remissions in all mice bearing HOC22 tumor, with 25% histopathol. confirmed cures, and produced marginal tumor growth delay against HOC8. These results indicate that ET-743 is a potent drug against ovarian carcinoma xenografts, being equally as active or more efficacious than DDP in the same tumor line. Our findings with human ovarian carcinoma xenografts justify clin. assessment of this drug with this tumor target.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 64 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:741343 HCAPLUS Full-text
DOCUMENT NUMBER: 128:34621
TITLE: In vivo immunosuppressive activity of some cyclolignans
AUTHOR(S): Gordaliza, Marina; Castro, M. Angeles; Miguel del Corral, Jose M.; Lopez-Vazquez, M. Luisa; San Feliciano, Arturo; Faircloth, Glynn T.
CORPORATE SOURCE: Lab. Quimica Farmaceutica, Facultad de Farmacia, Univ. de Salamanca, Salamanca, 37007, Spain
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(21), 2781-2786
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several podophyllotoxin-related cyclolignans, e. g. I, II and III (R1 = H, Ac, R2 = R3 = H; R1 = H, Ac, R2 = OH, OAc, R3 = H; R1 = H, Ac, R2 = H, R3 = OH, OAc), have been prepared and evaluated for their immunosuppressive (IMS) activity in the mouse allogeneic MLR in vitro test and in the in vivo techniques Graft vs Host Reaction (GVHR) and Skin Grafting (SG). The results obtained show that three cyclolignans fairly prevent splenomegaly in comparison with control animals and also promoted tolerance to grafting, being the first time that the in vivo IMS activity of cyclolignans is reported.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Full search history

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     (FILE 'HOME' ENTERED AT 09:13:32 ON 04 SEP 2007)

     FILE 'REGISTRY' ENTERED AT 09:14:06 ON 04 SEP 2007
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     FILE 'HCAPLUS, USPATFULL' ENTERED AT 09:17:18 ON 04 SEP 2007
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L3            64 SEA ABB=ON  PLU=ON  L2 AND (PY<2004 OR AY<2004 OR PRY<2004 OR
                 REVIEW/DT)
L4             6 SEA ABB=ON  PLU=ON  L3 AND DHB
                 E FAIRCLOTH G?/AU
L5            64 SEA ABB=ON  PLU=ON  ("FAIRCLOTH GLYNN"/AU OR "FAIRCLOTH GLYNN
                 T"/AU OR "FAIRCLOTH GLYNN T JR"/AU OR "FAIRCLOTH GLYNN
                 THOMAS"/AU)
                 E MARCHANTE M?/AU
L6             1 SEA ABB=ON  PLU=ON  "MARCHANTE MARIA DEL CARMEN CUEVAS"/AU
L7            64 SEA ABB=ON  PLU=ON  L5 OR L6
L8            57 SEA ABB=ON  PLU=ON  L3 NOT L7
L9            46 SEA ABB=ON  PLU=ON  L7 AND (CANCER? OR NEOTOM? OR NEOPLAS? OR
                 TUMOR? OR TUMOUR? OR PEPTID?)
L10           56 SEA ABB=ON  PLU=ON  L3 AND (CANCER? OR NEOTOM? OR NEOPLAS? OR
                 TUMOR? OR TUMOUR? OR PEPTID?)
                 D QUE L8
                 D IBIB ED AB
                 D L10 2-56 IBIB ED AB
                 D QUE L7
                 D L7 1-36 IBIB AB
                 SAVE TEMP L8 AUDHCPTX/A
                 SAVE TEMP L7 AUDHCPAU/A
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